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STUDIES ON PAIN

"SPREAD OF PAIN"; EVIDENCE ON SITE OF SPREAD WITHIN THE NEURAXIS OF EFFECTS OF PAINFUL STIMULATION

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NEW YORK

The crossed extension reflex shows that noxious stimuli can cause a spread of excitation that involves adjacent segments on the same and on the opposite side of the cord. Further, it has been suspected from the spread of deep pain from visceral disease that similar spread of excitation involving adjacent segments of the cord might occur. However, as far as can be ascertained, it has never been demonstrated that such spread involving sensation occurs at the segmental, rather than at a suprasegmental, level.[1]

The following data are evidence as to the site of occurrence in the neuraxis of the spread of excitatory processes from deep painful stimulation of high intensity.

CLINICAL DATA

F. W., a lawyer aged 48, had been found in 1940 to have a papilloma of the bladder, causing hematuria. The lesion was treated endoscopically by fulguration. With a recurrence of symptoms, he was admitted for the first time to the New York Hospital on March 20, 1944, where Dr. Allister McLellan performed a biopsy and fulguration of a papilloma of the bladder (presumably recurrent). The pathologic report was that of a transitional cell carcinoma. Because of persistent hematuria a suprapubic resection of the bladder was performed by Dr. McLellan on April 4.

Shortly after this operation the patient consulted Dr. Lewis Stevenson because of pain in the right hip and buttock, extending into the right lower limb as far as the foot. The limb also became progressively weaker, making weight bearing impossible. By July 1944 pain and weakness in the right buttock and the right lower lim were of such a degree that the patient was confined to bed and required occasional opiates. He did not complain of pain anywhere on the left side. The evidence indicated metastatic tumor involving the right hip joint and the right pelvic nerve plexus.

Roentgenotherapy failed to reduce the intensity of the pain; therefore, on Aug. 21 a chordotomy (section of the ventrolateral portion of the cord) was performed by Dr. Ray at the first thoracic segment on the left side only.

Examination on September 6 revealed that all pain sense (including deep pain perception) was lost below the nipple line on the right side to within 1 cm. of the midline. Temperature sense was lost in the same region. There was no demonstrable impairment of touch sense. The plantar responses were flexor in type, and there was no clonus. Sphincter function was normal. There was no sensory change on the left side.

After the operation the patient was free of all pain on the right side, but under certain circumstances he

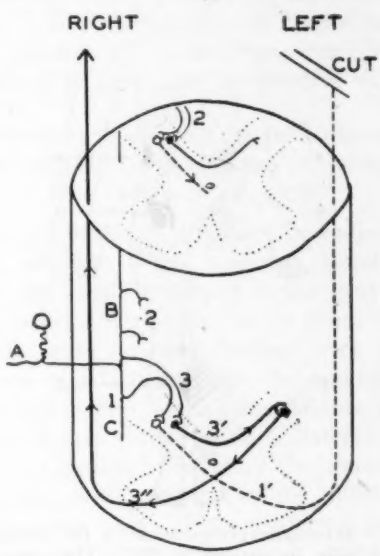

Fig. 1.—Schematic representation of the pathways for the "spread of pain" within the spinal cord. *A* represents primary sensory neuron, dorsal root ganglion; *B*, ascending branch of the sensory radicle, and *C*, descending branch of the sensory radicle. *1* is a collateral to the posterior horn of the nearest spinal segment. This connects with neuron *1'* which crosses to ascend in the opposite spinothalamic tract. *2* indicates collaterals to the adjacent segment, and *3*, collaterals to the posterior horn connecting with neuron *3'*, which forms part of the posterior commissure in crossing to the opposite posterior horn, where it arborizes to connect with neuron *3''*; this, in turn, crosses back to ascend the cord in the spinothalamic tract on the side of entry of the noxious impulses.

In patients F. W. and W. O. the spinothalamic tract was cut on the left side, and therefore the impulses from noxious stimulation ascended to the suprasegmental structures only on the right side.

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1. Wolff, H. G.: Some Observations on Pain, in Harvey Lectures, 1943-1944, Lancaster, Pa., Science Press, 1944, pp. 39-95.

experienced pain in the left buttock and, to a lesser degree, in the left heel. He reported that deep pressure over the trochanter and movement of the right hip induced pain on the left side.

Examination on September 9 revealed that when the position of the right lower limb was changed so as to move the diseased right hip or when heavy pressure was made over the trochanter of the right femur, the patient complained of pain of moderate intensity in the region of the left hip and buttock. He placed the palm and extended fingers of his left hand over the lateral portion of the left buttock to indicate the site and distribution of his pain. It was conceivable that moving the right limb stretched or displaced structures on the left side to produce pain. To resolve this doubt, the calf muscles on the right (diseased) side, far from the metastatic extensions, were vigorously squeezed in such manner as would produce intense deep pain in a normally innervated structure. No pain was experienced in the right calf, but a deep, aching pain was felt diffusely up and down the left leg as high as the hip, especially in the calf and heel. Similarly, vigorously squeezing the muscles on the right flank induced a diffuse ache over the left flank and the left side of the abdomen.

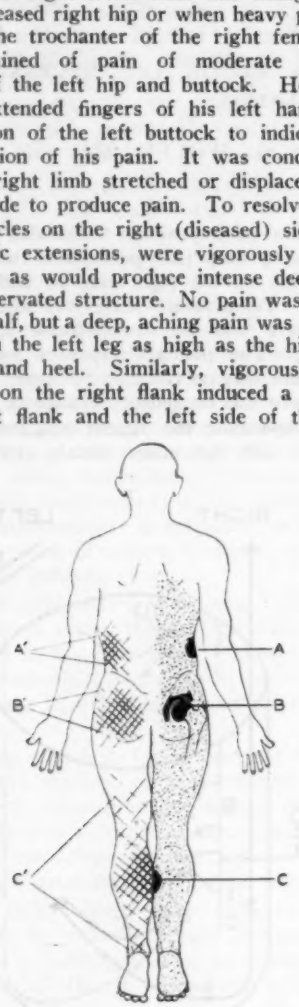

Fig. 2.—Schematic presentation of the analgesia and spread of pain in patient F. W. The stippled area shows the area of analgesia following chordotomy on the left side, approximately at the first thoracic segment. *A*, *B* and *C* are sites of noxious stimulation of high intensity on the analgesic side. *A'*, *B'* and *C'* are the diffuse areas of pain of low intensity perceived when areas *A*, *B* and *C* respectively were stimulated.

The following observations were made, the most intense pain being graded as 10 plus:

1. Deep pain of 6 to 8 plus intensity induced by compressing muscle in the left lower limb or on the left (normal) side of the abdomen did not induce pain anywhere on the right side.

2. Deep pain induced on the left (normal) side by movement of or deep pressure on the right (diseased) hip joint or by squeezing the right gastrocnemius muscle was only of 1 or 2 plus intensity and began about a half-second after the beginning of the noxious stimulation. The pain was diffuse, poorly localized and widespread. Also, it outlasted the period of stimulation by about half a second.

3. Stimulation, such as gentle rubbing of or pressure on the skin of the right (diseased) leg produced no pain on the left side. Only on deep noxious stimulation of the right (diseased) leg was pain perceived on the left side.

4. Noxious stimulation of the right leg and thigh (diseased side) by repeated pinprick did not induce pain sensation on either the right or the left side. The effects of noxious stimulation in producing burning sensation were not tested.

5. Noxious stimulation of low intensity, of the right (diseased) leg did not induce pain on the left side.

Comment.—The deep pain induced on the left side through movement of the diseased right hip did not result from secondary contractions of muscles of the left leg or buttock. With noxious stimulation of the nondiseased parts of the right leg, such as the gastrocnemius muscle, or the muscles of the abdomen and flank, pain was also experienced in corresponding areas on the left side.

Non-noxious stimulation of shorter or longer duration, such as gentle rubbing of or pressure on the skin and muscle of the right (diseased) leg produced no pain on the left side. Therefore the perception of deep pain in the left (normal) limb from noxious stimulation of the right limb could not have been due to the facilitating effects of non-noxious stimulation from the right side enhancing the perception of subthreshold noxious stimuli from the left side.

From a study of the following case similar observations on deep pain were made; in addition, it was possible to obtain data on cutaneous pain.

W. O., a linotype operator aged 41, was first admitted to the New York Hospital in April 1943, complaining of pain in the left side of his face and neck of about seven years' duration. Surgical exploration revealed a cholesteatoma at the base of the skull and in the region of the foramen magnum; the growth was removed. At the time of operation a small amount of the cholesterol crystal contents of the tumor escaped into the subarachnoid space.

The first of a series of readmissions to the hospital was in July 1943. The patient complained of almost continuous burning and aching pain in the sacrum and buttocks, which radiated down the posterior and lateral aspects of the thighs and legs into the ankles and toes. The pain during the ensuing year became worse on the right side than on the left. An exploratory laminectomy, in August 1943, had revealed radiculitis and arachnoiditis in the region of the cauda equina associated with aseptic meningitis. As a result of intrathecal injections of alcohol the patient had cutaneous hypalgesia of the foot and lower part of the leg on the right side.

By October 1944 the pain in the right leg had become unbearable and intractable, and a chordotomy at the first thoracic level, with section of the ventrolateral

region of the cord on the left side, was performed by Dr. Ray. After operation there was a defect in pain and temperature perception on the right side as high as the third thoracic segment, the site being slightly higher for temperature and slightly lower for pinprick. The patient felt no more spontaneous pain in his right leg, nor did he perceive pinprick, deep pain or heat or cold in this leg. However, when the gastrocnemius muscle was vigorously squeezed on the right (analgesic) side, he felt a diffuse, aching pain on the medial aspect of the thigh adjacent to the scrotum on the left (control) side. A metal tube containing hot water at a temperature of 80 to 90 C. applied to the skin just above the right knee was felt as burning pain in the left groin (control side). Also, heat applied to the right (analgesic) side of the abdomen was felt as burning pain on the left (control) side of the abdomen. The intensity and duration of stimulation necessary to produce this phenomenon were sufficiently great to result in diffuse reddening of the skin at the site of application.

Ice, when pressed against the skin for thirty to sixty seconds in the same areas, similarly induced on the left side a sensation of "burning" cold. All forms of noxious stimulation when applied to the left, or control, side elicited pain more promptly and of greater intensity than when applied to the right side and were identical in time and intensity with that described for F. W. Stimuli from warm and cold tubes at temperatures of 45 to 50 and 15 to 20 C. respectively, and from pinprick on the right (analgesic) side were not perceived on the left (control) side. Application of intense heat below the right knee produced no sensation on the left (control) side. About one week after the chordotomy the pain on the left side, which had been minimal at the time of admission, became progressively more intense.

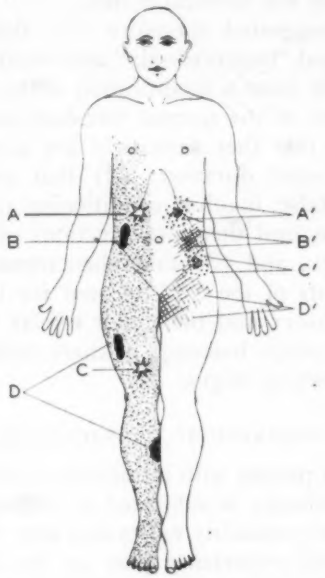

Fig. 3.—Schematic presentation of the analgesia and spread of pain in patient W. O. The stippled area shows the area of analgesia following chordotomy on the left side, approximately at the first thoracic level. *A* and *C* are sites of noxious stimulation of high intensity with heat (80 to 90 C.) on the analgesic side; *A′* and *C′* are the diffuse areas of burning pain of low intensity perceived when areas *A* and *C* respectively were stimulated; *B* and *D* are sites of noxious stimulation of high intensity with vigorous squeezing of muscle on the analgesic side, and *B′* and *D′* are the diffuse areas of aching pain of low intensity perceived when areas *B* and *D* respectively were stimulated.

Comment.—These considerations support the contention that excitation from noxious stimulation of high intensity spreads at the segmental level in the spinal cord. There it gives rise to effects which involve neurons in adjacent segments, as well as neurons that connect with the opposite side of the cord. Impulses are then conveyed headward through the intact spinothalamic tract and ultimately result in pain sensation.

The spread of pain after unilateral chordotomy from the diseased side to the side with normal sensation has been noted before in this clinic, but demonstration of the nature of this spread has been unsatisfactory because of the complicated illnesses of the patients in whom it was seen. Observations closely resembling those on F. W. and W. O. have been made on 2 other patients, but the patients whose cases are described here were especially astute and cooperative witnesses.

INTERSEGMENTAL AND INTRASEGMENTAL CONNECTIONS: POSTULATED PATHWAYS FOR "SPREAD OF PAIN"

Many collaterals of the sensory radicals conducting impulses from noxious stimuli, after entering the cord, terminate in the gray matter of the posterior horn close to the point of entry and come into synaptic relation with neurons the axons of which cross in the anterior commissure and ascend in the spinothalamic tract on the opposite side of the chord. Collaterals arising from the ascending branches of the sensory radicles connect with neurons in the substance of Rolando, other parts of the posterior horn and the central and intermediate gray matter. They terminate in the gray matter of segments of the cord adjacent to those of their entry.[2]

Furthermore, arising from the ascending and descending branches of the sensory radicle is another important group of collaterals. These collaterals establish synaptic relations in the dorsal horn with internuncial neurons the axons of which form the most dorsal part of the posterior commissure. At their terminations these axons ramify about cells in the dorsal horn on the opposite side of the cord. It may be accepted as a general principle that the collaterals of sensory radicles do not cross directly to the opposite

2. Ramón y Cajal, S.: Histology, Baltimore, William Wood & Company, 1933.

side of the cord.[3] The two sides are connected by means of internuncial neurons. Such internuncial chains supplement the shortest path for noxious stimuli to the suprasegmental structure. Moreover, if there is sufficient background of facilitation, together with sufficient intensity of stimulation, these less direct internuncial chains undoubtedly become passable.[4]

It is postulated from the observations on patients that there is a spread of excitation from the primary sensory neurons and their collaterals so as to involve (1) neurons in the segments of the cord of their entry and in adjacent segments that cross to the opposite side and ascend the cord in the spinothalamic tract, and (2) internuncial neurons that cross in the posterior commissure to stimulate neurons on the opposite side of the cord. The latter cross back to ascend the cord in the spinothalamic tract on the same side as the entering noxious impulses.

Each additional synapse introduced by internuncial neurons increases the resistance to the spread of excitation. Hence, it is conceivable that one or more intercalated neurons necessary for the passage of impulses from the side of entry to the other side of the cord introduce resistance which makes high intensity of noxious stimulation necessary for the spread of pain to the opposite side of the body.

Patient W. O. experienced pain before chordotomy from roots giving rise to both deep (aching) and superficial (burning) pain. These pains were far more intense on the right side but were present to a minimal degree on the left. After chordotomy burning and aching pains became more intense on the left side.

Before chordotomy patient F. W. experienced deep pain originating in the right, or abnormal, lower limb, but this was not associated with pain on the left, or normal, side. Several possible explanations suggest themselves: (1) The pain from the diseased (right) side was of such high intensity that the patient failed to perceive lesser pain on the opposite side; (2) section of the ventrolateral part of the cord on the left side, by removing suprasegmental inhibitory systems, altered the excitability of neurons in the cord and facilitated transmission at heretofore resistant synapses, and (3) spread of afferent impulses to the opposite side of the cord occurred as much before as after section of the spinothalamic tract, but with both spinothalamic pathways in operation there was interference with further transmission, which prevented these impulses from giving rise to sensation.

3. Lorente de Nó, R.: Personal communication to the authors.

4. Lorente de Nó, R.: Analysis of the Activity of the Chains of Internuncial Neurons, J. Neurophysiol. **1**:207 (May) 1938.

GENERAL COMMENT

Instances of spread of pain from deep noxious stimulation have been described and discussed elsewhere.[5] Suffice it to say here that this phenomenon results from spread of excitation within the cord, that such spread of excitation is mainly on the side of primary noxious stimulation, that direction of spread is somewhat more cephalad than caudal and that it does not equally involve all segments over which it spreads. Also, when the intensity of noxious stimulation is great, the opposite side may become involved.

From experimental evidence reported elsewhere [1] it has been inferred that surface "hyperalgesia" associated with deep noxious stimulation and pain, and perhaps some types of deep "hyperalgesia," result from reenforcement occurring within the cerebral cortex.

It is suggested therefore (1) that "hyperalgesia" and "hyperesthesia" associated with deep pain result from a modification within the cerebral cortex of the normal threshold surface impulses so that they seemingly are more intense and of longer duration; (2) that localization, true and false, involves conditioning or previous experience, and therefore functions of the cerebral cortex, and (3) that phenomena referable to segments of the cord account for the spread of the sensory and the motor effects associated with cutaneous burning, noxious impulses and pain of visceral origin.

THERAPEUTIC IMPLICATIONS

When a patient with intractable unilateral pain of high intensity is subjected to unilateral chordotomy the possibility exists that after the operation he will experience pain on the heretofore normal side. Unilateral chordotomy carries with it less hazard of serious damage to the cord than bilateral chordotomy; there is less likelihood of impairment of sphincter control, and, in the case of high cervical chordotomy, less danger to the respiratory mechanism is involved. For the relief of unilateral pain of low or moderate intensity by

5. McAuliffe, G. W.; Goodell, H., and Wolff, H. G.: Experimental Studies on Headache: Pain from the Nasal and Paranasal Structures, A. Research Nerv. & Ment. Dis., Proc. (1942) **23**:185, 1943. McLellan, A. M., and Goodell, H.: Pain from the Bladder, Ureter and Kidney Pelvis, ibid. **23**:252, 1943. Kunkle, E. C.; Goodell, H., and Wolff, H. G.: Observations on the "Ice Cream" Headache, unpublished data; cited by Wolff.[1]

chordotomy unilateral section is adequate and preferable, but for the relief of unilateral pain of high intensity bilateral section is superior to the unilateral operation.

SUMMARY AND CONCLUSIONS

Patients with hemianalgesia following high thoracic section of the ventrolateral portion of the cord on one side perceived pain on the normally innervated side of the body when the analgesic side was noxiously and intensely stimulated. Pain was not perceived on the analgesic side when the normally innervated side was noxiously stimulated.

It is inferred from these observations that the spread of pain of high intensity from one part of the body to adjacent regions on the same side and on the opposite side is a sequel of the spread of excitatory processes within the neural segments of the cord. Such spread of excitation via the neurons in the dorsal horns and the association pathways then incites impulses on the same and on the opposite side of the cord, some of which ascend the spinal cord to the suprasegmental structures, where neural function is ultimately expressed in the perception of pain. In short, the postulated spread of excitatory processes associated with pain of high intensity primarily involves the segmental structures, although secondarily the suprasegmental structures are implicated in perception, localization and reaction.

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EDEMA AND TROPHIC DISTURBANCES OF THE LOWER EXTREMITIES COMPLICATING PREFRONTAL LOBOTOMY

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Since April 1, 1942, 19 patients of the Milwaukee Sanitarium have had bilateral prefrontal lobotomies. All operations were done by two skilled and experienced neurosurgeons, who used the lateral approach described by Freeman and Watts.[1] Two of the older patients died of pneumonia while convalescing from the operation. Still another had acute collapse of a lung soon after the lobotomy but recovered. The very first patient to undergo the operation has since had one convulsion, but is regularly employed. None of the others, to our knowledge, has had convulsions. Immediately after operation all had rectal and vesical incontinence. Ten of the 17 survivors continue to have occasional sphincter accidents. One patient had a short, but intense, bout of diabetes insipidus during recovery from the procedure, but the complication was quickly controlled with posterior pituitary injection U. S. P.

In the course of our postoperative observations on these 17 patients, 8 have presented complications referable to the legs and feet. Six have had bilateral edema, in 4 of whom the edema was associated with tenderness. In 2 patients a tendency to edema of the feet and legs existed before the operation but was much aggravated after it; moreover, in these 2 patients bullae developed about the heels at points most vulnerable to pressure. After the operation 1 patient observed that her feet were swollen and required shoes a size larger. In another patient bullae developed on the heels but there was no edema.

It would seem that the incidence of these complications was greater than could be accounted for by mere chance. However, because the disturbances are usually mild and tend to pass away within a few months, they have doubtless often been overlooked. In a recent extensive review of the international literature on psychosurgery, Walker[2] did not report any cases of such complications. Freeman and Watts, in their many publications in this field, apparently have not discussed them.

Edema of the lower extremities is not particularly unusual among patients with mental disorders. It is more likely to be found in persons who are inactive, remaining in one position for long periods. It is not uncommon in elderly patients. We have also seen edema of the legs in men and women with mental disorders who were normally active and in whom it was indeed difficult to determine the cause. Obregia and associates[3] and de Giacomo[4] discussed some aspects of this subject.

For the most part, the patients in the present study were too ill to cooperate adequately in neurologic examination. There is much that one would like to know about some of them, especially whether the sensory system was disturbed. On April 1, 1944 Kindwall and Cleveland[5] completed a follow-up study on 15 of the surviving patients and have described elsewhere in detail the clinical effects of the operation. Some essential facts about the 8 patients with complications involving the lower extremities are given in the following clinical sketches. These cases are presented in the order of severity of the sequelae, complications in case 1 being the most disabling and distressing and those in case 8 the least so.

REPORT OF CASES

CASE 1.—F. M., a woman aged 53, who was divorced, had been a musician. She had progressed in school to junior college. Since the age of 20 she had been mentally ill more than half the time and had been in sanatoriums continuously since the age of 34. In 1929 she was examined at the Mayo Clinic, where, in addition to the psychosis, she was observed to have edema and cyanosis of the hands. Her psychosis had two

From the Milwaukee Sanitarium.

† Dr. Ziegler died on Jan. 8, 1945.

1. Freeman, W., and Watts, J. W.: Psychosurgery, Springfield, Ill., Charles C Thomas, Publisher, 1942.

2. Walker, E. A.: Psychosurgery: Collective Review, Internat. Abstr. Surg. **78**:1-11, 1944.

3. Obregia, A.; Dimolescu, A., and Sulica, M.: Physiopathogenesis of Aerosyndromes in Psychopathic Patients, Cluj. med. **15**:265-268 (May 1) 1934.

4. de Giacomo, U.: Su significanto di manifestazioni edematose osservate in olienati degenti negli ospedali psichiatrici, Riv. sper. di freniat. **61**:1090-1094 (Dec. 31) 1937.

5. Kindwall, J. A., and Cleveland, D.: Prefrontal Lobotomy: Fifteen Patients Before and After Operation, Am. J. Psychiat., to be published.

phases, which lasted a few days each and alternated more or less regularly. In one phase she was impulsive and yelled loudly, was profane, and sometimes obscene, and her remarks were critical and sneering. In the other phase she was fearful, acted as though hallucinated and withdrew entirely from others but was quiet. She did little work with her hands but read newspapers and listened to music over the radio. She had been given no shock therapy. Except for slight edema of the feet, physical and laboratory examinations revealed essentially a normal condition, and she had good control of the sphincters at all times. Her gait was normal.

Prefrontal lobotomy was performed on Sept. 19, 1943, and the cut was extended the following day. Pronounced incontinence of the bladder and rectum followed, and she has continued to soil herself occasionally since. Soon after the operation pronounced edema was observed in her lower extremities, extending nearly to the knees. The edematous areas were dry, pale and warm and did not pit easily; her feet were extremely tender. Soon after large bullae appeared on the backs of her heels, seemingly the result of pressure. Despite every precaution, such as elevation of the feet and relief from pressure, the bullae broke down and the resultant ulcers healed slowly; they resembled trophic ulcers in every way. Her toes assumed awkward positions and underwent rhythmic movements of an athetoid nature. For eight months she refused to walk and screamed whenever her legs or feet were touched. The edema and tenderness gradually subsided, and the ulcers healed. The accompanying photograph, taken May 1, 1944, shows the greatly improved condition of the extremities. On that date the ankle jerk was elicited, but not the knee jerk. Sensation seemed intact. The feet continued to be tender. Since May 1 she has been walking some and worn shoes. The psychosis has changed somewhat, but on the whole she has not improved. She remains in the sanatorium.

Fig. 1.—F. M.'s extremities as of May 1, 1944, more than seven months after lobotomy, when the edema had largely subsided, the ulcers on the heels had healed and she was beginning to walk, with help.

Case 2.—E. S., a very large man aged 44, married, had never had a regular occupation. He reached about the third year in college. At the age of 28 he began to have erratic and unstable behavior and was probably hallucinated. Since then he has been in many sanatoriums. He has expressed delusions, and occasionally what the "voices" have told him has sent him into a rage. He stared, held fixed positions and masturbated excessively. A course of insulin shock produced only temporary improvement. Slight edema of the feet and ankles had been present prior to the operation. At times he had soiled himself with urine. Some tremor of the thumb and the index finger had been noted. Except for these disturbances, physical and laboratory examinations revealed an essentially normal condition.

Lobotomy was performed on Jan. 11, 1944 and was completed four days later. After the operation the patient had an acute collapse of the lung. Marked incontinence appeared immediately, and he has continued to soil himself occasionally since. Soon after the operation pronounced edema of the lower extremities was observed. The edematous areas were pale, warm and dry, did not pit easily and were not tender. Within three weeks after the operation small bullae, seemingly due to pressure, appeared on the heels; they persisted from one to two months but did not ulcerate. Except for sluggishness, he walked without difficulty. After operation he showed a grasping reflex in both hands, which persists in mild form. The tendon reflexes were present. A Babinski sign was occasionally elicited in the left foot. The tremor persisted. Sensation appeared to be intact.

At the time of writing, seven months after lobotomy, the edema of his feet persists. He speaks only an occasional word but smiles at jokes and seems relaxed. Initiative is returning slowly. There have been no angry outbursts at the "voices," but he has admitted hearing them. He remains in the sanatorium.

Case 3.—R. M. R., a teacher aged 48, single, was graduated from college with Phi Beta Kappa honors. In early girlhood she became a worrier. Soon after the death of her father, when she was 35, she began to accuse herself of many things that were untrue. She worried over an unconsummated love affair and had fears which she could not understand. Since that time she has been in one sanatorium after another. Her spells of worry gave way to long periods of silence and uncommunicativeness, during which she stared and smiled; these spells were interrupted by short periods of excitement, in which she talked and listened to voices. In these excitements she was often noisy and sometimes combative, talked in an abusive, profane, surly manner and appeared on the point of frenzy. At the age of 41 she had edema of the ankles, which a salt-free diet dispelled. A full course of insulin shock therapy caused a gain in weight but gave only transitory improvement. At night she occasionally soiled herself with urine. Physical and laboratory examinations revealed an essentially normal condition.

Lobotomy was performed on Feb. 7, 1944, and the section was extended on March 9, 1944. Immediately after the first operation the patient was incontinent, and this has persisted, with occasional recurrences. Soon after the operation her left hand was observed to be edematous; this was attributed to intravenous medication or to her lying on it. Several weeks after the operation her feet were observed to be edematous, the left being more affected than the right. The

edematous areas were pale, dry and warm and pitted easily. At present her feet are very tender to pinprick or tickle. She limps a little on her left foot. In a neurologic examination, done on July 1, 1944, a slight grasping reflex was observed in both hands. She did not use the left hand as well as the right and did not swing her left arm much in walking, although muscular power in it appeared to be normal. The knee and ankle jerks were present. There were no signs of lesions of the pyramidal tract. The tissues of the left hand and forearm had a different texture from those of the right, feeling slightly more indurated.

The edema persists but responds to elevation of the extremities involved. The patient is still in the sanatorium in an inactive, quiet state, staring and smiling to herself. Unless provoked, she has no periods of excitement, and she adjusts herself better in a social group and requires less care.

Case 4.—M. J., a single woman aged 32, a college graduate and a teacher of Romance languages, had an insidious onset of the illness at the age of 21. By the time she was 26 she had lost interest in her surroundings, was aloof, easily offended, expressed bizarre ideas and had a pronounced energy defect. She often smiled to herself and at times told of the voices she heard. She was sometimes angry and combative, and it became necessary to place her under custody in a state hospital. Insulin and metrazol shock treatment produced improvement, which, however, did not endure. Her hands and feet were often cyanotic and cold. She had never soiled herself. Physical and laboratory examinations revealed an essentially normal condition.

Lobotomy was performed on Sept. 14, 1943. After the operation the patient had pronounced incontinence, which has since recurred at infrequent intervals. Soon after the operation her feet and legs, halfway to her knees, had a warm, pink edematous appearance, which lasted two to three months. During this time she walked as though her feet were tender and cried out in distress when slight pressure was applied to the ankles. Neurologic examination gave otherwise normal objective results.

Since the operation she is not aloof, laughs easily and is more sociable; however, at times she gets very angry. She must be urged to write letters or work in the occupational therapy room. She remains in the sanatorium.

Case 5.—F. L., a woman aged 42, had a private finishing school education. As a child she was "very good" but shy and tense. She married at the age of 23, had one child and was divorced several years later. At about the age of 30 she began to withdraw, even from her nearest relatives, and became careless about her personal appearance. At that time she expressed fears without being able to tell what made her afraid. Wherever she might be she would scream; in a store or restaurant she sometimes became disturbed and talked in a loud, accusing manner. At times she remained in bed all day. Before 1940 she had been in sanatoriums for brief periods; since that time she has been in an institution continuously. She stared, held fixed positions, smiled to herself and had occasional noisy outbursts of anger. She spoke little, was stilted in behavior and showed a pronounced energy defect. Full courses of insulin and metrazol shock therapy produced only transitory improvement. Although she sat about in fixed positions a great deal, she had no edema of the legs. She soiled herself at times. Except for secondary anemia and a moderate degree of undernourishment, physical examination and laboratory studies revealed an essentially normal condition.

Lobotomy was done on Feb. 22, 1944. Severe bleeding was encountered. Soon after the operation diabetes insipidus appeared, and the patient drank several quarts of water a day; this condition was controlled with posterior pituitary injection and has subsided. Immediately after the operation there was considerable incontinence, which soon decreased in severity but has continued to occur at intervals. Soon after the operation the feet and legs were slightly edematous for about three months and appeared dry, pale and tender. After the operation the patient became more animated and less completely preoccupied; her behavior, however, remains stilted. On the other hand, she does more things without being urged, and there have been fewer spontaneous outbursts of anger and irritability. She continues to live in the sanatorium.

Case 6.—K. M., a married woman aged 44, a high school graduate, began to show personality changes at the age of 40, when fatigue and depression caused her to resort to the excessive use of alcohol. She described feelings of unreality and inertia. Electric shock always dispelled these feelings and produced a hypomanic state; relapse, however, took place within a few weeks. Insulin shock only caused a gain in weight. She had an old ankylosis of the left hip joint. At no time in her life had she had trouble with sphincter control. Aside from the ankylosis of the hip, physical examination and laboratory studies revealed an essentially normal condition.

Lobotomy was performed on Nov. 3, 1943. Five days later the operation was extended. Incontinence largely subsided in one to two months but recurred occasionally for six months. Slight edema of the legs was observed soon after the operation; this disappeared within two to three months and caused no distress. The results of neurologic examination were normal while the edema was present. After the operation the patient became mildly elated, but not to such a degree as she had after electric shock therapy. She has retained this state and is getting on reasonably well at home save that, aside from pressure of speech, she lacks energy.

Case 7.—V. R., a single woman aged 28, completed three years of high school and attempted to become a clerk; she tried other occupations, as well, but fatigue prevented sustained work. At the age of 15 she began to be obsessed with her own tensions. She was jealous of her parents. Suicidal ideas were expressed many times. She often paced the floor at night saying, "I can't stand it." She had had no trouble with sphincter control. There was evidence of old thrombophlebitis in the left leg. Electric shock treatment gave only temporary relief. Mild insulin shock therapy only caused her to gain weight. Except for the thrombophlebitis, physical examination and laboratory studies gave essentially normal results.

Lobotomy was done on Jan. 28, 1944. Convalescence from operation was uneventful, and before the patient left the hospital the sphincters were under control. She wrote letters home three weeks after the operation. She noticed that her feet were swollen after the operation, and she was obliged to use shoes one size larger. Her feet were not tender. Neurologic examination gave normal objective results. She is now cheerful, easy-going and lacking in ambition but gets on at home with urging and guidance.

Case 8.—G. E., a high school boy of 16, was said to have presented a difficult feeding problem in infancy and may have been born prematurely. At the age of 14 he lost interest in school and was unable to do simple chores at home. These disabilities increased. Later, he talked to himself, twirled a lock of his hair most of the day and repeated the same remarks many times. Even his mother called him "silly," as he muttered in a low monotone, expressing bizarre ideas. Insulin and

electric shock treatments had little effect. He was undernourished, although he ate and slept well. Physical examination and laboratory studies revealed an otherwise normal condition.

Lobotomy was done on Jan. 14, 1944. The patient regained complete control of his sphincters within a month after the operation. Some bullae appeared on his heels. Neurologic examination gave normal objective results. He gained weight rapidly. At the time of this report his energy not only is greatly increased but is directed toward wider interests. He is making mediocre progress in a boarding school and is happy. No evidence of a psychosis is apparent.

The word "edema" derives from the Greek word οἴδημα, which means "swelling." It has come to have a special connotation, implying swelling due to excess water or fluid in the spaces between the tissue cells. In this it differs from the Latin word "tumor," which also means "swelling," but implies an overgrowth of tissue.

The simplest mechanism for the production of edema is a direct trauma to the tissues. Generalized edema is seen in the acute stages of infection, such as trichinosis. When the globulin-albumin ratio of the blood serum becomes too disordered, edema is likely to result. Damaged kidneys may be rendered unable to prevent albumin from passing into the urine; this favors the production of edema. Partial or complete circulatory obstruction, such as may occur in the veins of the leg, produces edema. Edema occurs also with cardiac failure, but not in every case. It is often seen after serious damage to the liver. Edema may be found in association with general starvation (cachexia) and is one of the commonest symptoms of vitamin B deficiency, as manifested in beriberi. Mild edema is seen at times with other forms of peripheral neuritis. A peculiar type of edema, which is called myxedema, appears in some patients with hypothyroidism. Lymphatic obstruction, too, causes an unusual type of edema known as lymphedema, commonly seen with elephantiasis. Although Quincke,[6] in 1882, and others before him, had described acute circumscribed edema, Strübing,[7] in 1885, first gave it the name angioneuritic edema, thus implying its relation to the nervous system and the blood vessels. Osler[8] first pointed out the hereditary tendencies of angioneurotic edema, which is said to occur intracranially on rare occasions. Urticarias are frequently related to allergy. A menstrual edema has been described. In 1892 Milroy[9] described an unusual form of edema of the lower extremities. He had observed it in families, the hereditary character indicating that some particular quality of the tissues predisposed to its occurrence.

These suggestions from clinical medicine point to elemental or primary factors in the pathogenesis of edema, among which should be mentioned (1) change in the permeability of damaged capillary walls; (2) changes in capillary pressure; (3) variations in the colloids of the blood serum; (4) lymphatic obstruction; (5) unknown hereditary factors, and (6) disturbances in central or peripheral innervation. Because of the nature of the complications under discussion, the possible relations between function of the nervous system and edema deserve further consideration.

The Peripheral Nervous System.—No work on this part of the nervous system has been more important than the pioneer demonstrations of Claude Bernard, who, in 1851, proved that the sympathetic nervous system subserves the function of vasoconstriction. Since his time many workers have shown the vasodilator and sweat-inhibiting effects of severing the sympathetic nerves from the central nervous system. One might conclude that after lumbar sympathectomy standing would increase the volume of the legs. (Standing has this effect in normal, healthy persons.) However, inconclusive evidence presented by Gambill, Hines and Adson[10] from a study of 4 patients about twenty days after lumbar sympathectomy for hypertension indicated that the standing volume of the legs was less after the operation than before.

The Central Nervous System.—For many years evidence has accumulated to suggest that the brain, and perhaps the brain stem and the spinal cord, may play a part in the production of edema. In 1867 Chevallier[11] wrote a thesis for the faculty in Paris on paralysis of vasomotor nerves in hemiplegia. In 1876 Eulenberg and Landois[12] came to the conclusion that there were

6. Quincke, H. I.: Ueber akutes umschriebenes Hautödem, Monatsh. f. prakt. Dermat **1**:129-131, 1882.

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8. Osler, W.: Hereditary Angioneurotic Edema, Am. J. M. Sc. **95**:362-367, 1888.

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10. Gambill, E. E.; Hines, E. A., and Adson, A. W.: The Circulation in Man in Certain Postures Before and After Extensive Sympathectomy for Essential Hypertension, Am. Heart J. **27**:360-380, 1944.

11. Chevallier, P. E.: De la paralysie des nerfs vasomoteurs dans l'hémiplégie, Thesis, Paris, no. 175, 1867.

12. Eulenberg, A., and Landois, L.: Ueber die thermischen Wirkungen experimenteller Eingriffe am Nervensystem und ihre Beziehung zu den Gefässnerven, Virchows Arch. f. path. Anat. **68**:245-271 and 489, 1876.

centers in the cerebral cortex near the motor centers for the arm and leg which influenced the vascular state of the extremities. In 1888 Gowers [13] reported similar observations, including the occasional presence of subcutaneous edema of the paralyzed part as a result of cortical or capsular lesions. In 1899 Parhon and Goldstein [14] studied 86 hemiplegic patients, 8 of whom had edema of the paralyzed hand. These authors did not attribute it to inactivity but stated that it was more probably related to hemianesthesia. Whenever edema has been found in association with hemiplegia it has usually been in the upper extremity. That edema and lesions of the central nervous system could be definitely related was suggested by Stone,[15] who, in 1929, reported his observations in the unusual case of a young girl who had had hemiedema with hemiplegia due to cerebral softening from embolus. Although he was unable definitely to locate an "edema center," after careful study of the patient's brain, his case, perhaps as much as any other reported up to that time, has helped to demonstrate a factor in edema referable to the central nervous system. In 1934 Kennard [16] presented experimental evidence for vasomotor representation in the cerebral cortex of monkeys. In 1935 Bucy [17] reviewed the literature and reported the clinical observations in an unusual case in which outspoken vasomotor changes were associated with paralysis of cerebral origin. In 1936 Luhan [18] found evidence of hemiedema in 15 of 100 cases of hemiplegia selected at random. In 7 cases, he gave detailed findings, including observations at necropsy in 2 of them. In his summary he said:

> . . . The cerebral lesion effects a tendency to localize actual or potential edema to the paretic extremities. . . . thus far the results of clinical studies which were checked with postmortem observations have not furnished any critical evidence for a cerebral vasomotor center of contralateral dominion.

In a summary and review of the literature in 1944 Kennard [19] accumulated additional clinical data from human subjects and brought together the experimental observations, including those of Fulton [20] and others, bearing on vasomotor representation in the cerebral cortex. The results of extirpation and stimulation experiments on monkeys and other animals have not been constant, and conclusions are difficult to draw. In general, it seems that area 6 (Brodmann) in monkeys contains within it elements capable of affecting the vasomotor system and the temperature of the contralateral extremities. This autonomic representation may extend somewhat into areas 4 and 8. The area for the leg is just anterior to the cortical motor centers for the leg and foot; the area for the arm, anterior to the cortical motor centers for the hand and arm.

The floor of the fourth ventricle, the brain stem and the hypothalamus have been shown experimentally to have an influence on the vasomotor system. Whether these areas are parts of association pathways or relay centers is not clear. Perhaps on the basis of such inconclusive evidence, Freeman and Watts [21] suggested that cutting the fasciculus cinguli might contribute to incontinence, in view of interruption of possible pathways between the cortex and the hypothalamus.

The motor cortex representing the foot appears to be a narrow zone anterior to the central sulcus, and at the very vertex of the hemisphere. The central sulcus is usually visible on the mesial surface of the hemisphere. About it on the mesial surface is the paracentral lobule, said to contain cortical sensory and motor representation for rectal, vesical and sexual structures. Green and Oldberg [22] and Erickson [23] have recently reported on patients with lesions of the paracentral lobule and adjacent structures and have reviewed pertinent literature bearing on it. The cortical center for the foot and the paracentral lobule are in close proximity. The rectogenitovesical structures themselves and part of the feet receive their innervation (sensory and motor) via centers in the sacral portion of the spinal cord. As might be expected, cortical

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14. Parhon, C., and Goldstein, M.: Contributiui la studiul contracturiei in hemiplegia, Romania med. **7**: 2-12, 1899.

15. Stone, T. T.: Hemiplegia with Hemiedema Due to Cerebral Softening, J. Nerv. & Ment. Dis. **69**: 651-660, 1929.

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17. Bucy, P. C.: Vasomotor Changes Associated with Paralysis of Cerebral Origin, Arch. Neurol. & Psychiat. **33**:30-52 (Jan.) 1935.

18. Luhan, J. A.: Hemiedema in Cases of Hemiplegia, Arch. Neurol. & Psychiat. **36**:42-56 (July) 1936.

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22. Green, J. R., and Oldberg, E.: Injuries of the Vertex of the Skull with Special Reference to the Paracentral Lobules of the Brain, Arch. Neurol. & Psychiat. **53**:89 (Jan.) 1945.

23. Erickson, T. C.: Erotomania (Nymphomania) as an Expression of Cortical Epileptiform Discharge, Arch. Neurol. & Psychiat. **53**:226 (March) 1945.

representations for such sacral neurons, so diverse in function, are very near each other.

In order to visualize the part of the cerebrum affected by the lobotomy, we went to the anatomic laboratory and cut through a brain in the plane of the lobotomy. On a sketch of the cut surface (fig. 2) we outlined the fields of the two chief operative approaches. The cut is presumed to be made in the white matter anterior to the premotor (extrapyramidal) cortex, near the plane of the coronal sutures.

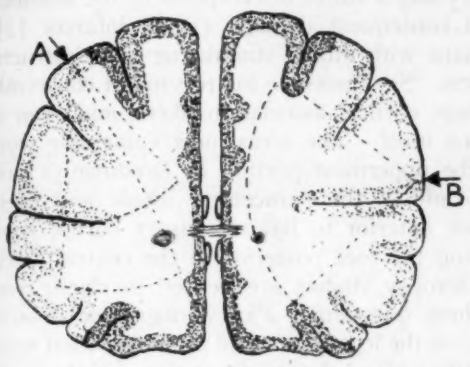

Fig. 2.—Drawing of the coronal surface of the brain at the plane of lobotomy. A few fibers of the most anterior portion of the corpus callosum are shown, with the tip of the anterior horn of the lateral ventricle at either side. The portion of the cortex which is shaded darker is that supplied by the anterior cerebral arteries, which are shown cut across below and above the corpus callosum. *A*, indicates the superior operative approach and the outline of areas which may be cut; *B*, the lateral operative approach and the outline of the area which may be cut.

From figure 2 the impression is gained that numerous association tracts, variable in length, including the frontothalamic, may be sectioned to some degree by the operation. The more specific nature and function of these tracts offer a fertile opportunity for investigation. If one may assume that man has cortical vasomotor representation in area 6, some of the fibers passing from such cells to the internal capsule may be injured directly by the lobotomy even when it is made fairly far anterior. From the position of these supposed vegetative centers, however, it might be assumed that more trophic disturbance would result directly from the lobotomy cut if it were made farther posterior. We have collected data that bear on this point.

At the time of operation it is customary for the surgeon to inject iodized poppyseed oil 40 per cent into the lobotomy cut and make a roentgenogram of the head to ascertain the plane of the lobotomy. This was done for all 17 of our patients. We have studied these roentgenograms and have classified the planes of the cut as anterior to, under, just posterior to or considerably posterior to, the plane of the coronal sutures. These data, together with those on the complications, including the persistence of incontinence, are presented in the accompanying table.

Correlation of Location of Lobotomy Cut (with Regard to Plane of Coronal Sutures) with Duration of Incontinence and Complications in the Extremities

Case No.	Plane of Iodized Oil in Lobotomy Cut as Seen in Roentgenograms of Skull in Relation to Plane of Coronal Sutures				Complications		
	Anterior	Under	Slightly Posterior	Considerably Posterior	Incontinence Lasting Less Than a Month	Incontinence Persisting Several Months	Extremities
1 F. M.	..	+	..	..	..	+	Severe tenderness and edema of legs and feet; bullae on heels
2 E. S.	..	..	..	+	..	+	Marked edema of legs and feet; bullae on heels
3 R. M. R.	..	..	..	+	..	+	Moderate tenderness and edema of feet; edema of left hand
4 M. J.	..	..	+	..	..	+	Mild tenderness and edema of legs and feet
5 F. L.	..	..	+	..	..	+	Mild tenderness and edema of feet
6 K. M.	..	+	..	..	..	+	Mild edema of legs
7 V. R.	..	+	..	..	+	..	Swelling of feet
8 G. E.	..	+	..	..	+	..	Bullae of heels
9 T. E.	..	+	..	..	+	..	None
10 S. M.	..	..	+	..	..	+	None
11 K. H.	..	+	..	..	+	..	None
12 L. W.	..	+	..	..	+	..	None
13 P. K.	+	..	..	..	+	..	None
14 T. O.	..	+	..	..	..	+	None
15 K. E.	+	..	..	..	+	..	None
16 L. E.	..	+	..	..	..	+	None *
17 B. M.	..	..	..	+	..	+	None *

* This patient had preoperative edema of the legs and feet, which disappeared after the operation because of increased activity (?) or trophic changes (?).

Of the 8 patients with complications referable to the legs, 6 had occasional incontinence of the bladder and rectum for considerably more than a month after the operation. Of 9 patients without complications of this sort, only 4 had such prolonged incontinence. Therefore it appears that complications in the legs may have something in common with persisting incontinence. However, the suggestion that the more posterior sections may be associated with such complications is not

entirely sustained by the data in the table. The lobotomy in case 17 was carried rather far posterior. Although the patient had persisting incontinence, at no time after the operation did she have edema of the legs. In fact, a slight preoperative edema of the legs disappeared subsequent to the operation. The lobotomy cut in case 1 was not posterior, and yet of all the patients she had the severest complications in the legs and persisting incontinence. There is, nevertheless, evidence in the table that the more anterior lobotomy is likely to be attended with less incontinence. These disconcerting facts, whatever their explanation may be, cause one to surmise that there may be anomalies of brain structure. The shape of the skull, too, may reveal discrepant relations between exterior landmarks and brain structure. The blood supply of the brain may be anomalous. There may be vasomotor representation in the cortex of a dual and antagonistic nature which overlaps considerably in one hemisphere. There may also be bihemispheral overlapping of function. Such possibilities could well account for the discrepancies in the results of experimental investigations on animals.

One must ever bear in mind the teaching of Hughlings Jackson that very different symptoms are to be expected from destruction than from stimulation of the nerve tissue. Alteration of the vascular supply of the brain may impair the functional integrity of structures at a considerable distance from the vascular defect. The portion of the cerebrum nourished by the anterior cerebral artery serves well to illustrate this point. This artery courses backward [24] over the mesial surface of the brain, sending branches laterally, upward and posteriorly to supply the gray and white matter of a narrow volume of the cerebrum adjacent to the mesial surface as far back as the parieto-occipital sulcus. Some branches of the anterior cerebral artery are said to supply the anterior portion of the thalamus, the basal ganglia and a part of the internal capsule. From a study of figure 2 it can be seen that small branches of the anterior cerebral artery might suffer interruption by the lobotomy, with consequent damage (small infarcts [?]), perhaps with mixed stimulating and destructive effects. Such possible infarcts might conceivably damage cortical association fibers, and even the cortex itself. The areas most vulnerable would be the uppermost portion of Brodmann's areas 8, 6 and 4, the paracentral lobule and mesial cortex anterior to it and sensory cortex representing the foot posterior to the central sulcus.

Necropsy studies are needed to clarify some of these questions. Plethysmographic observations on the legs before and after operation would doubtless give helpful information. If the operation were done on one side at a time, the intact side might serve as a control for the effects of operation. The anterior cerebral artery and its possible anomalies deserve renewed investigation. There are so many anomalies of the brain and skull that it would seem wise in dealing with the latter to remove a larger bone flap in preparation for the lobotomy, at present generally done through small openings in the skull.

We have not satisfactorily explained the clinical complications in the lower extremities in cases of prefrontal lobotomy. However, bedside observations on man and experimental investigations on monkeys point to areas in the brain lesions of which may produce edema and vascular and trophic disturbances. A more careful analysis in man of the functions of the cerebral cortex and subcortical structures nourished by the anterior cerebral artery may contribute greatly to the understanding of this problem. Milroy's disease (familial hereditary edema) and other obscure edemas of the feet and legs, as well as bullae, may be found to have a causative factor in the central nervous system, and it may well be discovered that enuresis is more than a defective habit, important as that can be.

The Milwaukee Sanitarium.

24. For charts of the blood supply of the brain, see Ranson's "Anatomy of the Nervous System" and Cunningham's "Text-Book of Anatomy."

ORGANIC PSYCHOTIC SYNDROMES OCCURRING DURING ELECTRIC CONVULSIVE THERAPY

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In electric convulsive therapy the first clinical improvement is frequently followed by an acute psychotic picture which is an organic reaction caused by the treatment. Not only are such disturbances of practical importance for the correct application of electric convulsive therapy, but they have many theoretic implications of great interest. The much discussed impairment of memory is the most constant, but never the only, organic mental symptom during electric convulsive therapy. Careful examination will reveal equally early symptoms in the emotional sphere. In a fair number of patients more dramatic syndromes develop. These always have certain characteristic features which permit their diagnosis as organic psychotic reactions implanted on the psychosis for which the patient is being treated; they disappear within one or two weeks after the last treatment. Their misinterpretation often leads to untimely cessation of treatment or, more frequently, to its unnecessary prolongation because of symptoms which are mistaken for residual manifestations of the patient's original illness.

Their symptoms repeat the great variety of acute syndromes occurring as organic reaction types. Early the patients show difficulty in concentration, have various physical complaints and manifest what has been called "organic neurasthenia." All intellectual functions, grasp as well as memory and critical faculty, are impaired; fatigability, circumstantiality and tendency to perseveration become obvious. Later, Korsakoff-like pictures may develop. The patient is disoriented in space and time, is incoherent in speech and action and shows aphasic-apraxic symptoms. Associations become poor. Often, disturbances of affect dominate the picture. Some patients become euphoric; others, fearful; still others go from bewilderment to a severe furor. Patients in psychomotor excitement aggravated by delusional fears and hallucinations make senseless attempts to escape, trying to go through windows and disregarding injuries. A typical delirium is not infrequent. Patients who never had hallucinations have vivid hallucinatory experiences. They experience entire scenes, which are changeable and may stir their fear to a panic. When treatment is continued in spite of such productive symptoms, these manifestations usually are replaced by a simple dementia. At this stage the patient may wet and soil himself, wander around aimlessly or become underactive and pass into a vegetating existence.

It is common to all these manifestations that they clear up one or two weeks after the last treatment; even the most dramatic symptoms often disappear suddenly on the fifth or sixth day. There is always complete amnesia for these syndromes even if the content of the pretreatment psychosis is well remembered.

Sometimes patients who had reached a quiet state of dementia recover by going again through a productive phase, with disturbed behavior, assaultiveness, delusional fears and hallucinations.

A. C., aged 18, with dementia precox, catatonic type, and no history of hallucinations, received twenty electric convulsion treatments. He became free from symptoms after four treatments but later showed an organic type of reaction, which finally resulted in a state of quiet, silly confusion. Five days after the last treatment he became acutely disturbed, had a hunted look, accused himself of being a murderer and saw preparations for his execution. An interview revealed the organic type of these symptoms, which were accompanied by complete disorientation. No further treatment was given, and five days later full recovery took place.

The correct interpretation of these late manifestations of an organic reaction is of special importance, for if they are mistaken for a relapse of the original psychosis they may lead to unnecessary reinstitution of treatment.

A few of the organic mental symptoms may be discussed in more detail. The impairment of memory follows the pattern seen in all organic diseases of the brain and extends gradually from more recent to remote recollections. This is well exemplified by a patient who was born in Russia, lived for many years in Germany and has been

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Some observations mentioned in this paper were made by the author at the Pilgrim State Hospital, Brentwood, N. Y.; director, Dr. Harry J. Worthing.

in this country for fifteen years. He first lost his English and was able to speak only German. After more treatments he spoke only Russian, without realizing that nobody understood him. After treatment had been discontinued, ability to speak the languages returned in the same sequence. The condition of this rather unproductive patient, with paranoid schizophrenia, who also went through an acute hallucinosis during the treatment, has now been in full remission for two years, without showing any memory difficulties.

The disorientation of these patients involves not only time and place but also person. They do not realize their defect and improvise explanations, but are not productive in confabulations. When the organic episode has cleared up, it becomes obvious that no actual loss has occurred. Therefore, when intense treatment is necessary to achieve results,[1] the occurrence of an organic reaction is no reason that treatment should be discontinued for fear of mental sequelae. Psychologic studies have confirmed the opinion that no actual loss of memory is demonstrable in patients after a course of electric convulsive therapy.[2] The learning ability in particular was found unimpaired. A physician suffering from a depression and showing a Korsakoff picture during the treatment was able, a few months later, to pass a difficult examination.

A case especially rich in its organic symptoms may be described briefly.

D. B., a woman aged 20, a quiet hebephrenic patient, without delusions or hallucinations, went through the first nine treatments uneventfully, with only slight confusion. After the tenth treatment she began to hallucinate, showed signs of psychomotor agitation and talked incessantly and incoherently. A sample of her uninterrupted productions follows: "Tonight I saw little satans on the door, but God was awfully nice to me. I wanted to go to bed with Tommy. I had Germans here tonight killing me. I am awfully sexually inclined. The Germans were shooting at me, but I beat them all up. I do read the Bible. I saw many seraphims on the door." After two more treatments she became quiet, stood around, looked silly and embarrassed and talked hardly at all. Four days after the twentieth, and last, treatment this stuporous condition began to disappear. She looked fearful, cried and again, two days later, became acutely disturbed; she would dance, sing, tear her clothes, roll over the floor, bite other patients, soil and smear. During the following day the picture was exactly that shown during the actual treatment, which was characterized by visual hallucinations and uninhibited sexuality. Again, two days later, i. e., nine days after the last treatment, she was perfectly quiet, well behaved, oriented and reasonable.

It is common experience in electric convulsive therapy that the clinical improvement occurs during the first five treatments. When new psychotic symptoms appear during the subsequent convulsions, they are usually signs of an organic reaction. They often show features reminiscent of the illness suffered by the patient prior to treatment; thus, a patient with a manic-depressive psychosis is more likely to show an organic reaction with affective tainting, and a schizophrenic patient, more schizophrenia-like symptoms. However, a differential diagnosis of the original psychosis and the organic reaction occurring during the treatment is usually possible: In schizophrenic patients the occurrence during electric convulsive therapy of cloudiness, disorientation, affective incontinence and efforts on the part of the patient to establish a better contact with the physician will suggest the diagnosis of an organic reaction. The hallucinations of an organic reaction are more vivid, and often changing, and the patient's affective response to them is stronger than is usual in schizophrenia. Apparent changes from a quiet hebephrenic state to one of acute excitement, or from a catatonic stupor to a productive paranoid state, with hallucinations and delusions, is generally a transient organic reaction. Permanent transitions from one subtype of schizophrenia to another are rare and were not seen in any of my patients receiving shock therapy.

The recognition of an organic reaction in patients with manic-depressive psychoses is sometimes more difficult. A depressed patient who has been free from symptoms after four treatments may become apprehensive or worried about physical complaints after a few more treatments. Simultaneous signs of a slight confusion and the different type of depression, characterized by a more superficial fearfulness, reveal the organic reaction. Therefore, it would be a mistake to continue treatment with the expectation of recovery from this reaction, which will clear up spontaneously when treatment is discontinued. The often mentioned "hypomanic reaction" after treatment of a depression is usually a transitory organic syndrome, characterized by silly euphoria and great suggestibility. On the other hand, a manic patient treated twice, two years apart, showed on both occasions a short organic reaction of depressive tainting. True shifting from one phase of the manic-depressive psychosis to the other was seen only in patients who had shown such alternation prior to treatment.

1. Kalinowsky, L. B.: Electric Convulsive Therapy, with Emphasis on Importance of Adequate Treatment, Arch. Neurol. & Psychiat. **50**:652 (Dec.) 1943.

2. Zubin, J., and Barrera, S. E.: Effect of Electric Convulsive Therapy on Memory, Proc. Soc. Exper. Biol. & Med. **48**:596, 1941. Sherman, I.; Mergener, J., and Levitin, D.: The Effect of Convulsive Treatment on Memory, Am. J. Psychiat. **98**:401, 1941.

A predisposition to psychotic reactions of organic type can be assumed. In cases of symptomatic psychoses occurring during infectious and toxic diseases, the presence of such a predisposition was assumed from observations that the same patient reacted to repeated infections each time with a psychosis. During electric convulsive therapy, although all the patients have some organic symptoms, the degree varies considerably; and in several instances both the intensity of the reaction and the type of symptoms remained the same during different courses of treatment. One patient with three courses of therapy reacted each time with a severe Korsakoff syndrome after as few as four treatments. Several patients with two long courses of therapy showed a surprising scarcity of organic symptoms during each course. Although such experiences make the existence of predisposing factors probable, none could be defined except that patients in the involutional period of life seem to become more confused. Very old patients, in whom arteriosclerotic or senile changes in the brain could be expected, showed surprisingly little organic reaction, although their confusion after each individual treatment was longer than that in younger patients. There is no relation between the intensity of the organic reaction described here and that of the confusion after each individual convulsion which was discussed in other reports.[3] There is no evidence that psychotic patients are more susceptible to organic mental symptoms than neurotic patients. Aside from the impression that catatonic patients especially often failed to show organic signs, no relation between the degree of severity of organic symptoms and the type of disease could be established.

The organic psychotic syndromes during electric convulsive therapy offer almost experimental conditions for studies on "pathoplastic" influences of various factors on the structure of a psychosis.[4] Thus, the type of symptoms in psychoneurotic patients is usually in accordance with their schizoid or cyclothymic personality traits. It is equally understandable that psychotic patients show organic reaction types with affective or schizophrenic features in accordance with their original mental illness. Exceptions to this rule are of particular interest: One schizophrenic patient in two series of treatments showed the same depressive-hypochondriacal reaction, followed by a manic-euphoric picture; she was of pyknic type, had some affective symptoms, and in the beginning her illness had been diagnosed as a manic-depressive psychosis by several psychiatrists. Another exception was a patient of pyknic type with clearcut catatonia who after fifteen treatments showed a manic-like organic reaction with grandiose ideas. The influence of constitutional factors was equally well demonstrated by the manic syndrome of a neurotic patient of pyknic type whose sister had a manic-depressive psychosis.

The organic reactions during electric convulsive therapy have interesting implications with respect to the question of the symptomatic psychoses during toxic-infectious diseases and confirm the view [5] that the symptoms of an exogenous psychosis do not depend on the noxious agent which caused it. Electric convulsive therapy shows that the same agent can produce clinical pictures of the greatest variety. It is not the damaging agent but constitutional and other factors within the patient which determine the picture. Only certain symptoms are constant in all organic reactions and are uninfluenced by personality factors.[6]

The prognosis of the organic syndromes during electric convulsive therapy is as favorable as the prognosis of other symptomatic psychoses. The intensity of the reaction has no bearing on the duration. Disappearance of symptoms is sudden. Complaints of memory impairment over a longer period are not more frequent in patients with severe organic reactions than in patients with mild ones.

The question arises whether the organic mental symptoms as such, or pathophysiologic changes supposedly producing them, are necessary for results in electric convulsive therapy. Reports on remissions in psychotic patients during and after head injuries [7] and experiences with psychosurgery suggest that organic interference with cerebral function is likely to improve a psychosis and may also be the effective agent in shock therapy. It seems, however, that clinical manifestations of an organic reaction type are not necessary for therapeutic results. In 50 schizophrenic patients, each treated with twenty convulsions and studied with this question in mind, no relation between the degree of severity of the organic mental symptoms and the therapeutic

3. Löwenbach, H., and Stainbrook, E. J.: Observations on Mental Patients After Electric Shock, Am. J. Psychiat. **98**:828, 1942.

4. Birnbaum, K.: Der Aufbau der Psychose, Berlin, Julius Springer, 1923.

5. Bonhoeffer, K.: Die symptomatischen Psychosen im Gefolge von akuten Infektionen und inneren Erkrankungen, Leipzig, F. Deuticke, 1910.

6. Hoch, P. H.: Personality Factors in Alcoholic Psychoses, Psychiatric Quart. **14**:338, 1940.

7. Guttmann, E.: Suicidal Head Injuries, J. Ment. Sc. **89**:85, 1943.

results was seen: Daily treatments which invariably led to severe confusional states did not increase the therapeutic effect. Good results with schizophrenic patients reported [8] to have followed such "confusional treatment" are also obtainable with the same number of treatments given at greater intervals.[1] Further evidence against the influence of organic symptoms is furnished by the two facts that patients under electric convulsive therapy generally improve after four treatments, i. e., before they show even a memory defect, and that nonconvulsive responses produce confusion but no therapeutic results.

Organic psychotic reactions are seen not only with electric convulsive therapy but with insulin treatment. The Korsakoff picture is frequent after "protracted coma." Slight hypomanic states, as well as Sakel's [8c] "activation of the psychosis" during insulin treatment, were shown to be organic reactions.[9] This is important for the study of the common factor in the various shock methods which might be concerned in the cerebral damage, though not necessarily in the degree of its clinical expression.

It is undeniable that the frequency of organic syndromes is an unpleasant side effect of electric convulsive therapy. Rarer application of treatment (twice a week) diminishes but does not prevent them and prolongs the treatment unduly. Occipital application of the electrodes [10] or administration of oxygen during the treatment [11] did not prevent confusion in a series of patients whom my colleagues and I treated in this way. It actually had been anticipated that the organic symptoms were not produced by the area of application of the current and its intensity but were the result of the repeated convulsive state.

Therapeutic use can be made of the organic reaction itself. The recommendation of occasional electric convulsion treatments as an adjunct to psychotherapy of neurotic patients [12] is based on the organic symptoms of relaxation, disinhibition and euphoria, which loosen the patient's tension and thus make him more accessible to psychotherapy. Improvement in neurotic patients, which neither in type nor in degree is comparable to the results obtained with the psychoses, can often be achieved simply by producing an organic reaction.[13] Another use of the organic "blurring" was made when withdrawal symptoms were prevented in 2 patients with morphine addiction by producing an organic reaction with three treatments on two successive days prior to sudden withdrawal of the drug.

A thorough knowledge of the organic psychotic syndromes during electric convulsive therapy is of the greatest practical importance, for their misinterpretation may lead to inappropriate application of the treatment. Patients who improve rapidly from a depression but who after more treatments show uncertainty and bewilderment of an organic type are often considered as still depressed and are unnecessarily subjected to further treatment. Psychotic symptoms during electric convulsive therapy which follow a period of improvement are usually organic in type; actual relapses do not occur during the treatment but only after its discontinuation. In cases in which a deep but quiet organic reaction clears up by passing through a phase of excitement, unnecessary initiation of a second course of electric convulsive or insulin treatment is often a consequence of the failure to recognize the organic nature of the acute episode. Another mistake is discontinuation of treatment because of an organic reaction which is taken for aggravation of the patient's condition. In cases of schizophrenia in which twenty, or even more, treatments are needed, such discontinuation is often responsible for inadequate treatment. It should be realized that in favorable and unfavorable cases alike, the outcome of electric convulsive therapy can be determined only two weeks after the last convulsion, i. e., when the organic reaction has definitely cleared up.

SUMMARY

A great variety of organic psychotic episodes can be observed during a course of electric convulsive therapy. The appearance of new symptoms during such treatment is usually indicative of an organic reaction. The correct interpretation of these syndromes is of paramount importance for proper planning of electric convulsive

8. (*a*) Löwenbach, H.: Electric Shock Treatment of Mental Disorders, North Carolina M. J. **4**:123, 1943. (*b*) Neymann, C. A.; Urse, V. G.; Madden, J. J., and Countryman, M. A.: Electric Shock Therapy in the Treatment of Schizophrenia, Manic Depressive Psychoses and Chronic Alcoholism, J. Nerv. & Ment. Dis. **98**:618, 1943. (*c*) Sakel, M.: The Pharmacological Shock Treatment of Schizophrenia, translated by J. Wortis, Washington, D. C., Nervous and Mental Disease Publishing Company, 1938.

9. Erb, A.: Zur Psychopathologie der hypoglykämischen Zustände bei Schizophrenen, Ztschr. f. d. ges. Neurol. u. Psychiat. **162**:65, 1938.

10. Sogliani, G.: Elettroshockterapia e cardiazolterapia, Rassegna di studi psichiat. **28**:652, 1939.

11. Holovachka, A.: Oxygen in Electro-Shock Therapy, J. Nerv. & Ment. Dis. **98**:485, 1943.

12. Selinsky, H.: The Selective Use of Electroshock Therapy as an Adjuvant to Psychotherapy, Bull. New York Acad. Med. **19**:245, 1943.

13. Kalinowsky, L. B.; Barrera, S. E., and Horwitz, W. A.; Electric Convulsive Therapy of the Psychoneuroses, Arch. Neurol. & Psychiat. **52**:498 (Dec.) 1944.

therapy. Treatment is often unnecessarily continued because of symptoms which are no longer an expression of the original disease, or it is prematurely interrupted because transient organic episodes are taken as an aggravation of the patient's illness. They constitute one of the reasons why not the purely mechanical application of electric convulsive therapy but only thorough acquaintance with the psychiatric manifestations during the treatment can lead to its successful employment.

These organic reactions offer almost experimental conditions for the study of the various factors which determine the type of symptoms in a "symptomatic" psychosis. They have interesting implications for a number of neuropsychiatric problems.

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ORIGIN OF THE SPIKE AND WAVE PATTERN OF PETIT MAL EPILEPSY

AN ELECTROENCEPHALOGRAPHIC STUDY

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It is interesting that despite the current emphasis which has been placed on the electroencephalographic detection of cortical lesions and the successful identification of the epileptogenic focus for a certain group of patients displaying generalized convulsions, no such demonstrable cortical lesions have been shown to constitute the focus for attacks of petit mal epilepsy. The hypothesis that the focus for petit mal epilepsy may be subcortical, and therefore not capable of being identified by the usual electroencephalographic technics, receives support from evidence cited by Penfield and Erickson [1] (page 138). These authors reported a case of petit mal epilepsy for which the focus was identified by implanting electrodes in the region of the interpeduncular space. Records from the electrodes were obtained which demonstrated a local discharge at this point, and certain characteristics of the seizure were reproduced by stimulating this area.

The data to be presented in this paper constitute further evidence of the subcortical origin of petit mal seizures. This evidence is derived from electroencephalograms and is concerned with (*a*) the distribution of the spike and wave pattern of petit mal epilepsy after almost complete section of the corpus callosum and (*b*) the time of onset of the spike and wave pattern as recorded from a series of widely separated scalp leads.

METHOD

The technic of recording was similar to that in general use in electroencephalographic laboratories. The electrodes were small German silver cups attached to the scalp convex side up. They were secured in place with colloidin and filled with electrode jelly through a small central hole. Flexible wires led from the scalp buttons to a set of selector switches so arranged that each pair of leads could be connected to any of six independent amplifiers. The recorders consisted of moving iron piece speaker elements adapted for use as ink writers. The natural period of the pens was about 40 cycles per second, and their overshoot was reduced to a minimum by electromagnetic damping. Either monopolar or bipolar leads were employed, the choice depending on circumstances. During the test the patient reclined on a cot in a semidarkened, electrically shielded room. The amplifier and the recording apparatus used in this investigation were designed by Dr. A. C. Young.

RESULTS

The records from which the data were assembled all showed repetitive complexes clearly containing the spike and wave pattern, which has been found pathognomonic of petit mal epilepsy (Gibbs, Lennox and Gibbs [2]). The position and size of the spike with reference to the wave were variable. The frequency of the waves varied from 2 to 4 per second. No attempt was made to differentiate petit mal seizures, larval petit mal attacks and petit mal variants, either on a clinical or on an electrical basis.

In presentation of the results, the term "sequence" is used to refer to the complete set of petit mal waves associated with a single outburst. The term "signal" is frequently used when it is desired to refer to a single spike and wave.

Effect of Section of the Corpus Callosum on Distribution of the Spike and Wave Pattern.—If the spike and wave pattern of petit mal epilepsy were initiated at a discrete cortical site and the abnormal discharge then spread to other cortical regions, involvement of the contralateral hemisphere would be expected to occur via the fibers of the corpus callosum. This expectation was borne out for the spread of the train of abnormal waves set up by the brief local stimulation of the monkey cortex in the experiments of Erickson.[3] He found that section of the corpus callosum resulted in confinement of the abnormal waves to the hemisphere which contained the site of the original electrical stimulation. Similarly, in the

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1. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Ill., Charles C Thomas, Publisher, 1941.

2. Gibbs, F. A.; Lennox, W. G., and Gibbs, E. L.: Localizable Features of the Electrical Activity of the Brain in Petit Mal Epilepsy, Am. J. Physiol. **116**:61 (March) 1936.

3. Erickson, T. C.: Spread of the Epileptic Discharge: An Experimental Study of After-Discharge Induced by Electrical Stimulation of Cerebral Cortex, Arch. Neurol. & Psychiat. **43**:429 (March) 1940.

case of the single action potential spike initated by local cortical stimulation (Curtis[4]) it was found that section of the corpus callosum resulted in confinement of the observed electrical response to the ipsilateral hemisphere.

It should therefore be possible to answer the question whether the petit mal attack was incident in the cortex by a study of the cortical distribution of the spike and wave pattern in the postoperative electroencephalograms of the patient after section of the corpus callosum. If the spike and wave pattern was obtained from both hemispheres after section, its appearance might be regarded as presumptive evidence that the complex in question had not originated in the cortex but had spread up into both hemispheres from a subcortical focus. Van Wagenen has performed section of the corpus callosum in a number of epileptic patients.[5] Fortunately, I was able to secure postoperative records on 2 of these patients during petit mal seizures. Representative spike and wave sequences taken from these records appear in figures 1 and 2.

The patient whose electroencephalogram appears in figure 1, a man aged 21, had been subject to epileptic attacks since the age of 5 years. At the time he was seen at the electroencephalographic laboratory he was having numerous petit mal seizures and only occasional grand mal attacks. The petit mal seizures were of from three to thirty seconds' duration and involved lack of orientation, with no other clinical signs[5b] (page 975). The portion of record presented in figure 1 *C* was chosen from numerous spike and wave sequences appearing in his postoperative records, taken on five different occasions. This portion was selected because it presents tracings from monopolar leads from six widely separated loci, and its value suffers from the fact that the spike and wave pattern is not well pronounced in the lead from the right precentral area. However, scrutiny of the original record, simultaneous time coordinates being taken into account, clearly establishes the presence of the petit mal pattern in this lead.

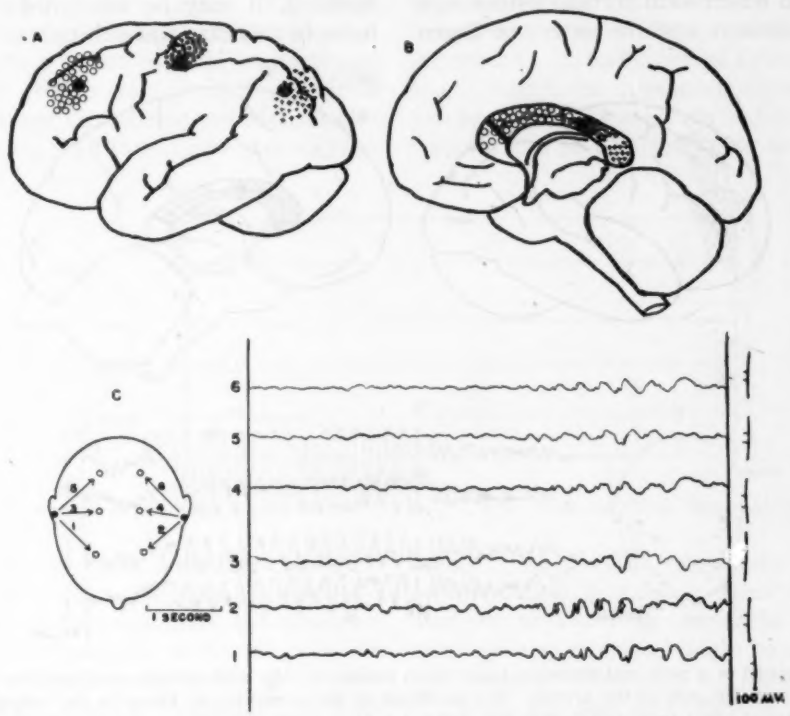

Fig. 1.—The record of a petit mal wave sequence taken from patient E. L., with partial section of the corpus callosum, as indicated by marks at the ends of the arrow. The positions of callosal fibers, as shown in *B*, are related to the cortical areas indicated by the same code in *A*. The large black dots in *A* represent the cortical projection of the electroencephalographic scalp leads. *C*, postoperative records, showing spike and wave sequences.

4. Curtis, H. J.: Intercortical Connections of the Corpus Callosum as Indicated by Evoked Potentials, J. Neurophysiol. **3**:407 (Sept.) 1940.

5. (*a*) For a preliminary report of this work, see Van Wagenen, W. P., and Herren, R. Y.: Surgical Division of Commissural Pathways in the Corpus Callosum, Arch. Neurol. & Psychiat. **44**:740 (Oct.) 1940. (*b*) The cases of these 2 patients are described in detail in a second article (Akelaitis, A. J.; Risteen, W. A.; Herren, R. Y., and Van Wagenen, W. P.: Studies on the Corpus Callosum: III. A Contribution to the Study of Dyspraxia and Apraxia Following Partial and Complete Sections of the Corpus Callosum, ibid. **47**:971 [June] 1942).

In general, it may be said that bilaterally symmetric leads show in-phase spike and wave complexes of similar shape. Since the section in this case was not complete, it is important to identify the extent of the destruction of interhemispheral connections via the corpus callosum in terms of the areas from which the electroencephalographic tracings were recorded. *A* and *B* of figure 1 attempt to clarify this question. It has been assumed that the monkey cortex and the human cortex are comparable with regard to the arrangement of fibers in the corpus callosum according to the cortical area from which they are derived. The diagrams in *A* and *B* (fig. 1) were made on the basis of the experiments of Sunderland,[6] in which local cortical lesions were produced in monkeys and the extent of degeneration of fibers in the corpus callosum was investigated histologically. The position of the lesions as related to the scalp leads employed in the electroencephalographic study are represented in a drawing of the human cortex in figure 1 *A*. The large black dots refer to the approximate position of the electroencephalographic leads as projected on the underlying cortex. A code similar to that used to indicate the separate lesions is employed in figure 1 *B*, showing their representation as fibers in the corpus callosum. Figure 1 *B* also indicates the extent of the section of the corpus callosum as stated in the surgeon's operative notes. The entire area between the heavy lines at the ends of the arrow was included in the section.

It is apparent that little or no interference with conduction with respect to the precentral and parietotemporal areas would be expected. The callosal connections for the frontal area were seriously interfered with; therefore it might be reasonable to expect the disappearance or pronounced attenuation of the response in one frontal area if it is assumed that the spike and wave signal has a local cortical origin and spreads from one frontal area to the other via callosal fibers. Since the spike and wave complex appears in both frontal leads, as shown in figure 1, it may be concluded that the initial focus in this case was subcortical.

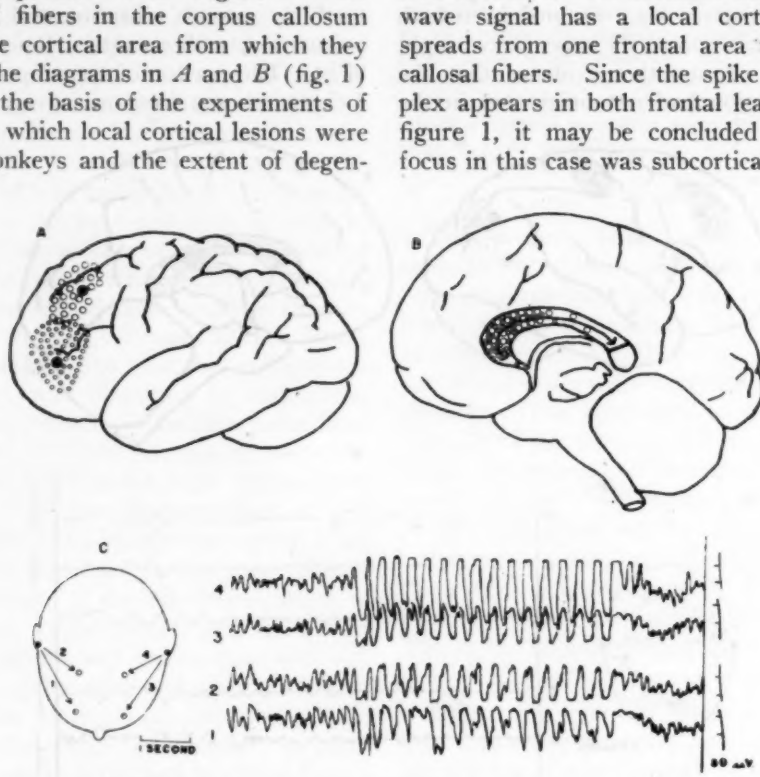

Fig. 2.—The record of a petit mal sequence taken from patient A. M., with partial section of the corpus callosum, as shown by marks at the ends of the arrow. The positions of the commissural fibers in the corpus callosum (*B*), in terms of the cortical areas from which they are derived (*A*), are identified by use of a code; large black dots in *A* represent the cortical projection of the electroencephalographic scalp leads. *C*, postoperative records.

Figure 2 presents comparable data in the second case. The seizures of this patient, a man aged 26, began at the age of 15 years. In addition to petit mal attacks, he was also subject to grand mal seizures, which developed with no preliminary warning or aura [5a] (page 751). It will be evident from figure 2 *B* that the callosal section was considerable in this case, extending from the anterior commissure to within 1 cm. from the tip of the splenium. The fornix was also divided just anterior to the foramen of Monro. It is probable, therefore, that the fibers of the corpus callosum for the prefrontal and frontal areas were sectioned in their entirety (granted a fundamental analogy between the human and the monkey cortex). Since the spike

6. Sunderland, S.: Distribution of Commissural Fibers in the Corpus Callosum in the Macaque Monkey, J. Neurol. & Psychiat. **3**:9 (Jan.) 1940.

and wave complex appears simultaneously in all four leads, the possibility of an initial focus in the frontal or the prefrontal area of the cortex is excluded.

There remains the question whether the focus might reside in some other cortical area and spread via rapidly conducting axons to the sites from which the leads were taken. The existence of rapidly conducting intrahemispheric and interhemispheric axons has been established by recent physiologic evidence. Curtis,[4] by electrical means, and McCulloch and Garol,[7] by local application of strychnine found that the stimulation of areas 5 and 6 and a small part of area 9 set up potentials which could be recorded from many areas on the opposite hemisphere. The short latencies between the stimulus and the response at mutually distant points indicate transmission via axons of the corpus callosum as the mode of conduction. Dusser de Barenne and McCulloch [8] presented evidence that axonal connections exist between areas in the same hemisphere subserving sensation in a particular part of the body.

These observations necessitate the consideration of two other possible modes of initiation and spread of the petit mal complex. The first possibility is that a cortical focus exists in those specific areas (that is, areas 5 and 6 and a part of area 9) which have connections via the corpus callosum to multiple areas on the opposite hemisphere. According to this view, the simultaneous appearance of the signal in the frontal and prefrontal leads depends on the conduction of the wave complex from its origin, say area 5 of the right hemisphere, to the corresponding area of the left hemisphere via the corpus callosum and the subsequent rapid bilateral conduction to the frontal and prefrontal areas by way of the multiple callosal pathways. This possibility may be excluded by examination of Sunderland's map of the distribution in the corpus callosum of the fibers from areas 5, 6 and 9. It becomes apparent that the section of the corpus callosum has destroyed all connections of the corpus callosum from these regions.

The second possibility is that of a focus in the occipitoparietal area, conduction to the corresponding area of the other hemisphere through callosal fibers of the intact splenium and, finally, intrahemispheric conduction to the frontal and prefrontal areas. In order to examine this possibility, a record was obtained from the patient with leads connected as shown in figure 3. An attempt was made to induce a petit mal attack by hyperventilation. Although no attack was induced, single petit mal complexes appeared in the record. Examination of figure 3 shows that single complexes appear simultaneously in the two prefrontal-frontal leads and that no petit mal complex can be detected in the occipital-parietal leads. The possible explanation based on the assumption of an occipitoparietal focus can therefore be regarded as untenable. A somewhat similar mode of spread might be suggested based on the supposition that the initial focus was in the temporal area and that the petit mal signal was conducted through the anterior commissure to the opposite hemisphere and then spread forward by means of intrahemispheric axon paths. This proposal may be disposed of, since figure 3 shows that the petit mal signal may appear simultaneously in the right and the left prefrontal-frontal leads but only in the left precentral-temporal lead.

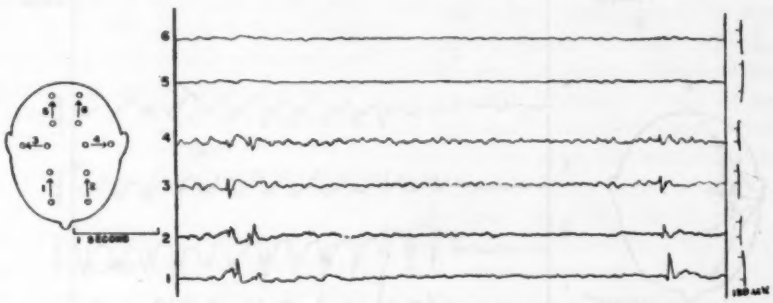

Fig. 3.—The record of petit mal waves for patient A. M., with leads placed as shown in the diagram.

Since other possible modes of spread of the spike and wave signal from the cortical focus have been shown to be incompatible with the electroencephalographic data available for this patient, it is concluded that the initial focus in this particular subject is subcortical. The proposal that in general petit mal epilepsy originates at a subcortical level receives support from a consideration of the time of onset of the spike and wave sequence as measured in the electro-

7. McCulloch, W. S., and Garol, H. W.: Cortical Origin and Distribution of Corpus Callosum and Anterior Commissure in the Monkey, J. Neurophysiol. **4**: 555 (Nov.) 1941.

8. Dusser de Barenne, G. S., and McCulloch, W. S.: Functional Organization in the Sensory Cortex of the Monkey, J. Neurophysiol. **1**:69 (Jan.) 1938.

encephalograms of a group of patients examined at the laboratory.

Simultaneous Onset of the Spike and Wave Pattern in Multiple Leads.—Study of the time of onset of the spike and wave signal at cortical sites at a distance from each other was carried out by analysis of 275 distinct sequences in the records obtained from 21 patients with petit mal epilepsy. The records of 13 patients showed a simultaneous onset of the signal in all leads employed and for all sequences recorded. The records of 6 patients showed a simultaneous onset in some patients and 3 sequences for the other, it might be supposed that if a greater number of attacks had been recorded simultaneity of onset might also have been demonstrated for these patients. It may therefore be said that for 18 of 21 patients sequences could be selected showing a simultaneous appearance of the spike and wave signal for all leading arrangements investigated.

Figure 4 shows records of the petit mal sequences for 3 patients and demonstrates the simultaneous appearance of the signal in multiple lead sets. In figure 4 *A* the appearance of the

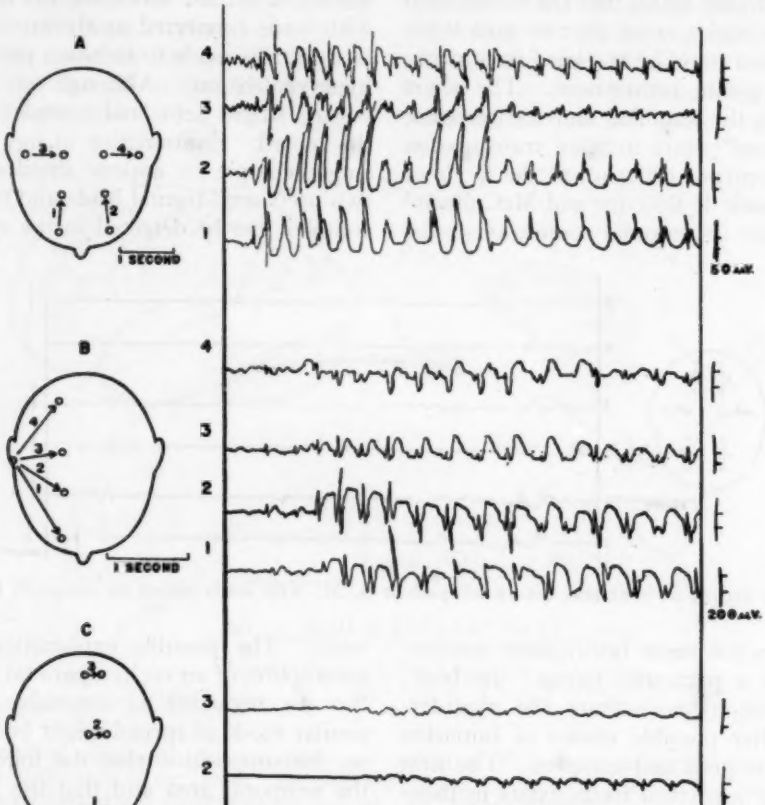

Fig. 4.—Record showing the simultaneous onset of the spike and wave complex in multiple leads of the electroencephalogram, arranged as shown in the diagrams. Simultaneous coordinates are shown at the right margin. Calibrations of amplitude are designated by the horizontal lines on the pen coordinates.

of the sequences and delayed appearance in one or more leads in other sequences. For 5 of the 6 patients it was found that with any given leading arrangement in which appearance of the signal was delayed in one or more leads in a particular sequence, another sequence could be discovered which showed simultaneous appearance of the signal in all leads. Of the entire group of 21 patients, the records of 2 showed delayed appearance of the signal in one or more leads for all the sequences recorded. Since there were available for study only 1 sequence for 1 of these

petit mal sequence is shown to occur about one second after the beginning of the record. If the simultaneous ordinates shown at the right of the figure are considered, it can be seen that the initial spike is simultaneous in all four bipolar leads. Leads 1 and 2 show an in-phase slow wave; leads 3 and 4, an out-of-phase slow wave. This finding taken alone is compatible with the assumption of either (*a*) a single source located centrally with respect to the uppermost buttons of each pair of leads or (*b*) a greater amplitude of signal at the uppermost buttons, although

the petit mal complex appeared simultaneously in all areas from which leads were taken. It is probable that the latter assumption is the correct one, since another record obtained from this patient, using monopolar leads from the same areas of the scalp, showed the simultaneous appearance of the petit mal signal in all leads. Figure 4 *B* demonstrates simultaneity of onset with a monopolar system of leading. Records with bipolar leads, which were also taken on this patient, showed simultaneous appearance of the spike and wave signal in all leads.

Figure 4 *C* shows the beginning of a petit mal sequence as recorded from buttons placed only 3 cm. apart. When the differences in potential from points so close together are recorded and scalp leads are used, rather small excursions of the pen are to be expected. For this reason it is difficult to distinguish the first spike and wave in lead 2. Examination of the original record enables one to distinguish a small spike in lead 2 which occurs simultaneously with the first spike in leads 1 and 3. The tracings in *C* have been included since, with such a short distance between leads, the electrical condition would favor the recording of differences of potential originating from the cortex as distinct from differences in potential arising from deep cortical or subcortical regions.

The simultaneity of onset of the spike and wave pattern as recorded from relatively distant scalp leads has been noted in the literature (Gibbs and Gibbs,[9] Jasper,[10] pages 412 and 425). The observation is presented in this paper in order to examine its meaning in relation to the site or origin of petit mal epilepsy.

If the electroencephalogram permitted the measurement of the time of onset to within a millisecond and showed simultaneous initial spike and wave signals at a number of widely separated points, the possibility of a discrete cortical origin could be dismissed at once. Unfortunately, the first condition was not satisfied, for at least two reasons: (1) The fast paper speed of 4 cm. per second, even with the greatest care in the determination of simultaneous coordinates of the different pens, did not permit the estimation of time much closer than to ± 10 milliseconds; (2) the shape of the spike and wave complex as recorded from scalp leads is sufficiently rounded and distorted by local leading conditions as to make it difficult to select any point of the complex for which simultaneity to within 1 millisecond could be determined, even though cathode ray technic was used.

Since the figures in the text establish coincidence only to about ± 10 milliseconds, they may be regarded as evidence for the noncortical origin of the petit mal complex only if it can be shown that the rate of spread of the dysrhythmia from a cortical focus would be expected to be slow in terms of the minimum measurable time difference.

Repetitive cortical dysrhythmias produced in monkeys as an after-discharge, following local electrical stimulation of the cortex (Erickson [3]), show that the time occupied by the march of the paroxysmal waves from the artificial cortical focus to the farthermost point in the motor strip of the opposite hemisphere was of the order of seven seconds. Injection of thujone into the femoral vein of rabbits (Adrian and Matthews [11]) caused a paroxysmal type of cortical discharge, spreading at a rate of about 10 cm. per second.

The more rapid rates of spread for action potential spikes (Curtis and Bard,[12] Curtis [4]) which are conducted from one hemisphere to the other, with latencies of ten to forty milliseconds as measured from the shock artefact to the wave crest, do not apply to the case in hand, since (*a*) the petit mal complex is not a simple action potential spike and (*b*) in the experiments previously cited the spike was conducted via the corpus callosum. It has been shown that an intact corpus callosum is not a necessary condition for the simultaneous appearance of the spike and wave complex at comparable loci in the two hemispheres.

It may therefore be urged that the petit mal complex is much more analogous to the slowly spreading "after-discharge" waves than to the more rapidly conducted spikes and that the determination of simultaneity from the measurement of the electroencephalograms is sufficiently accurate to constitute evidence for the noncortical origin of the spike and wave complex.

COMMENT

In the presentation of the experimental data, two assumptions have been made without explicit acknowledgment, namely, that the petit mal complex derives from a single focus (without prejudice as to the cortical or the subcortical origin) and that the nerve elements in the cortical layer are active in the production of the electrical complex.

9. Gibbs, F. A., and Gibbs, E. L.: Atlas of Electroencephalography, Cambridge, Mass., Lew A. Cummings Company, 1941, p. 221.

10. Jasper, H. H.: Electroencephalography, in Penfield and Erickson,[1] chap. 14.

11. Adrian, E. D., and Matthews, B. H. C.: The Interpretation of Potential Waves in the Cortex, J. Physiol. **81**:440 (July) 1934.

12. Curtis, H. J., and Bard, P.: Intercortical Connections of the Corpus Callosum as Indicated by Evoked Potentials, Am. J. Physiol. **126**:473 (July) 1939.

Unless the first assumption is valid, any consideration of the location of the focus becomes meaningless. An alternative to the origin in a single focus is an alteration in the chemical environment of the cortical cells, mediated presumably by a change in the composition of the circulating blood and causing a general response of all the cells.

The simultaneity of the onset and of the disappearance of the signal at loci distant from each other makes the latter alternative unlikely. An even more powerful argument against this theory of the nonspecific genesis of the petit mal waves exists in the identity of pattern frequently observed in bilaterally symmetric leading arrangements. Figure 5 (*A* and *B*) shows examples of this identity in pattern. Rosenblueth and Cannon[13] sought to explain the widespread synchronization of the self-sustained cortical response by showing that all cortical regions have similar time constants and by postulating a shifting cortical pacemaker. According to this view, no single specific cortical pacemaker exists, and the area which fires first discharges over facilitated neuronal paths to all other areas. Without commenting on the validity of this interpretation, one should point out that important differences exist between the responses which the authors recorded after electrical stimulation of the cortex and the petit mal sequences under discussion. The synchronization that is cited by these experimenters exists only after the gradual cortical spread of the responses has taken place. The synchronization of the spike and wave complexes may exist from the very beginning of the cortical

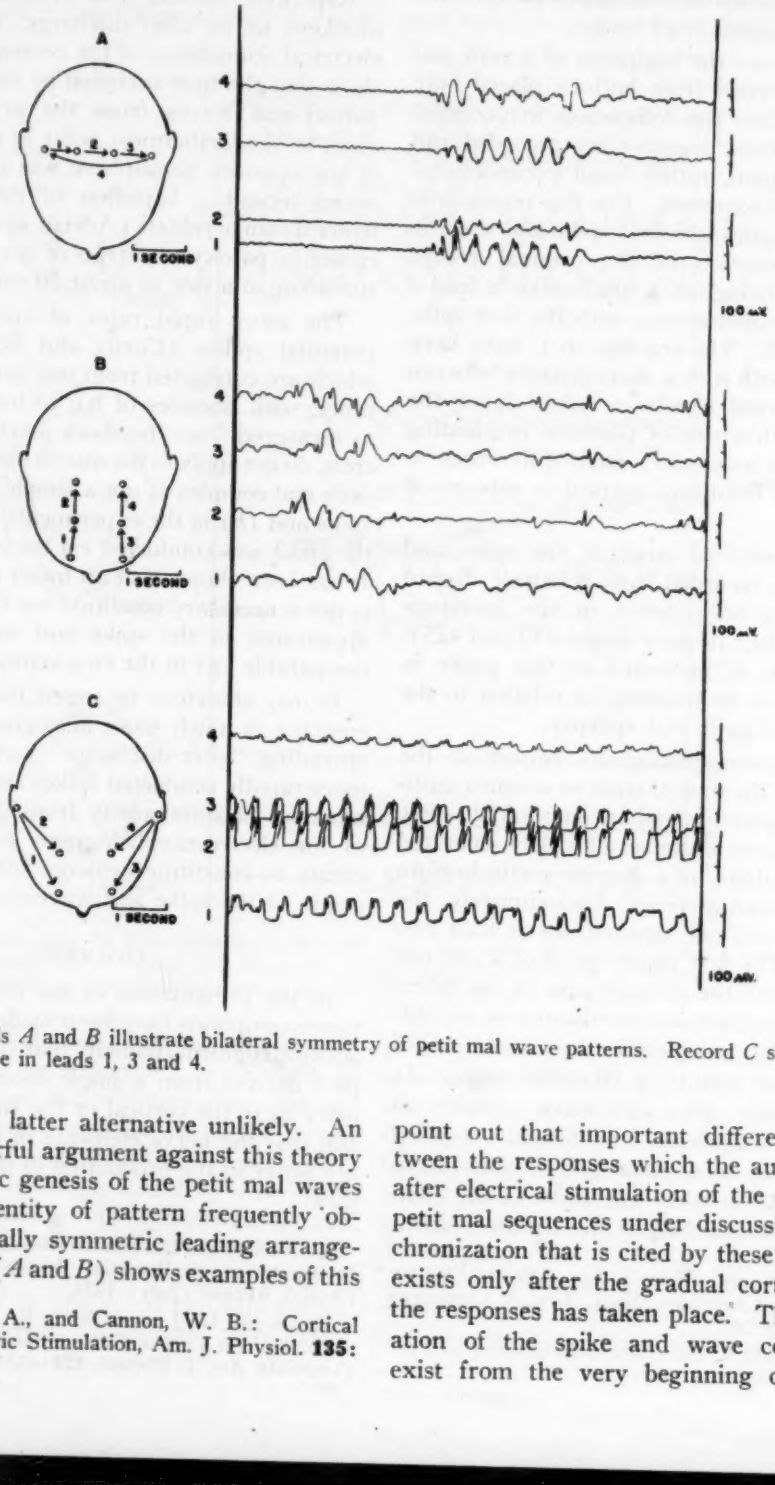

Fig. 5.—Records *A* and *B* illustrate bilateral symmetry of petit mal wave patterns. Record *C* shows a "dropped-out" petit mal wave in leads 1, 3 and 4.

13. Rosenblueth, A., and Cannon, W. B.: Cortical Responses to Electric Stimulation, Am. J. Physiol. **135:** 690 (Feb.) 1941.

response and therefore cannot be said to depend initially on facilitated intracortical conduction paths.

Figure 5 *C* shows a transient exception to the commonly observed bilateral symmetry of the electrical response. Here the lead from the right prefrontal area shows a "dropped-out" wave. This is duplicated in the left frontal lead but not in the right frontal lead. It is important to note that the wave following the omitted wave appears simultaneously in all four leads. The phenomenon illustrated in figure 5 *B* is suggestive of a transient conduction block such that no response occurs to one excitation wave proceeding from a pacemaker, although the next excitation wave passes through. Such a phenomenon would certainly not be expected if the local cortical areas were responding independently to a chemical change of the kind tentatively postulated.

The second assumption, i. e., that the cortical cells in the neighborhood of the leads produce the petit mal pattern, as distinct from a condition in which the excitation is restricted to a central oscillator and the electrical signal is led through the cortex, can be less satisfactorily established for all cases. There can be no doubt that in specific instances the local cortex is producing the signal. Such instances include cases in which the spike and wave complex does not appear simultaneously in all leads or in which the patterns in two bilaterally symmetric leads are transiently dissimilar, as appears in figure 5 *C*.

Any general theory of the genesis of the paroxysmal discharge associated with petit mal epilepsy must therefore take into account the apparent simultaneity of onset in distant cortical regions, the fact that the corpus callosum is not a necessary neural link in the conduction to all parts of the cortex and the necessity for the existence of some pacemaker in order to synchronize the discharge and to determine the small variations in pattern frequently found to be identical in symmetric leading arrangments.

If a subcortical pacemaker is postulated for all paroxysms of the petit mal type, certain limitations restrict the choice of a structure in which the focus may be tentatively placed. This structure must contain projection fibers with a widespread cortical distribution. The conduction paths from the pacemaker to the cortex must be approximately equal for all the cortical areas in question. The structure must display a degree of topical localization, since the recorded discharge may be confined to a discrete cortical locus. The postulated neuronal conduction paths cannot include motor neurons as an essential link, since no motor phenomena are encountered in the usual petit mal attack.

The thalamus presents itself as a possible site for such a pacemaker. It has frequently been postulated that the thalamus plays an important role in the maintenance of the spontaneous electrical activity of the cortex. Dusser de Barenne and McCulloch [8] showed that the spontaneous electrocorticogram of the monkey is changed or abolished after chronic cutting of the corticothalamic and thalamocortical fibers. Morison and Dempsey [14] showed that electrical stimulation of the thalamus in cats under light anesthesia induced with pentobarbital sodium may produce 8 to 12 per second cortical waves of widespread distribution, resembling the normal spontaneous cortical waves.

This observation is evidence that a close functional connection exists between the thalamus and the cortex. That topical representation exists in the thalamus is well known. It is, therefore, not unreasonable to assume the existence of the anatomic framework for the conduction of paroxysmal discharge from the thalamus to the cortex, with negligible small differences of latencies for mutually distant regions of the cortex. The hypothesis further requires that a discrete thalamic pacemaker discharge, that the excitation rapidly spread to the site of contralateral representation in the thalamus and that the paroxysmal involvement of such thalamic areas as are essential for "total" cortical representation occur before the characteristic spike and wave appears in any part of the cortex. In this connection, it may be said that Rosenblueth and Cannon [13] were unable to produce self-sustained discharges by electrical stimulation of the thalamus in monkeys under anesthesia induced with a compound of chloral hydrate and dextrose. Dempsey and Morison [15] found, however, that a single shock to the medial thalamus of a lightly anesthetized cat may produce a burst of 8 to 12 per second cortical potentials, lasting for two or three seconds. It is not clear in this case whether the after-discharge should be regarded as solely intracortical or intrathalamic as well. There is no question that the depth of anesthesia and the frequency and strength of the stimuli applied may be important experimental factors in the further elucidation of this point.

14. Morison, R. S., and Dempsey, E. W.: A Study of Thalamo-Cortical Relations, Am. J. Physiol. **135**:281 (Jan.) 1942; The Production of Rhythmically Recurrent Cortical Potentials After Localized Thalamic Stimulation, ibid. **135**:293 (Jan.) 1942.

15. Dempsey, E. W., and Morison, R. S.: The Interaction of Certain Spontaneous and Induced Cortical Potentials, Am. J. Physiol. **135**:301 (Jan.) 1942.

SUMMARY

The postoperative records of 2 patients with nearly complete section of the corpus callosum show "petit mal" sequences displaying a simultaneous onset in bilaterally symmetric leads. Since conduction between the two hemispheres via axon paths in the corpus callosum has been destroyed, the existence of a cortical focus cannot be assumed in these particular patients. It is most likely that in the records of patients without section of the corpus callosum in which a similar simultaneous onset was displayed, conduction of the signal did not occur through the corpus callosum and that the source of this signal was subcortical in these patients, as well as in the patients subjected to operation.

The thalamus or the hypothalamus is considered as a tentative site for the pacemaker of the spike and wave complex.

Radiation Laboratory, Massachusettts Institute of Technology.

Dr. William P. Van Wagenen cooperated in the taking of records from the hospital patients used in this investigation.

ELECTROENCEPHALOGRAPHIC STUDY OF PREFRONTAL LOBOTOMY

A STUDY OF FOCAL BRAIN INJURY

LIEUTENANT ROBERT COHN (MC), U.S.N.R.

Because of the high incidence of head wounds (and resultant cerebral damage) sustained by casualties in the war, present interest in the study of injury to the brain has become great. Clinical studies, in which the electroencephalogram was used as an indication of disturbance in cerebral physiology following cranial lesions, have been extensively reported.[1] Much experimental laboratory work has been done to support and supplement these clinical data.[2] Despite the general excellence of these studies, many problems remain for solution because of the deficiencies inherent in the methods employed. The most apparent defect in the clinical work is that few of the subjects were known to the investigators prior to the post-traumatic study. In the experimental work animals were used as subjects; consequently, the results were not directly applicable to the phenomenon of cerebral injury as seen in man.

The electroencephalographic work presented in this report was carried out in conjunction with therapeutic prefrontal lobotomy.[3] The importance of this work to the general study of injuries to the brain becomes apparent when one considers the following conditions:

1. Controlled, well circumscribed and clearly defined lesions of the brain were produced.

2. Fifteen subjects were studied before and for a year or more after injury to the brain.

3. All studies were on human beings.

From the Blackburn Laboratory, St. Elizabeths Hospital, Washington, D. C.

This work was aided in part by a grant from the Supreme Council, Thirty-Third Degree Scottish Rite, Masons of the Northern Jurisdiction, U. S. A.

1. Jasper, H. H.; Kershman, J., and Elvidge, A.: Electroencephalographic Studies of Injury to the Head, Arch. Neurol. & Psychiat. **44**:328-350 (Aug.) 1940. Williams, D.: Electroencephalogram in Chronic Post Traumatic States, J. Neurol. & Psychiat. **4**:131-146 (April) 1941. Harris, H. I.; Wittson, C. L., and Hunt, W. A.: Value of Electroencephalogram in Prognosis of Minor Head Injuries: Preliminary Report, War Med. **4**:374-379 (Oct.) 1943.

2. Williams, D., and Denny-Brown, D.: Cerebral Electrical Changes in Experimental Concussion, Brain **64**:223-238 (Dec.) 1941.

3. Freeman, W., and Watts, J. W.: Psychosurgery, Springfield, Ill., Charles C Thomas, Publisher, 1942.

In this discussion on prefrontal lobotomy no attempt will be made to evaluate the clinical effectiveness of the method in the treatment of the psychoses.[3] The only concern is: What is the electroencephalographic evidence of cerebral damage, and in what way can such knowledge be utilized in the interpretation of electroencephalograms in cases of less precisely placed lesions (accidental trauma)?

METHOD

This report is based on the study of 30 human beings (civilians) with various psychiatric conditions, whose ages ranged from 20 to 65 years. Each subject underwent bilateral therapeutic prefrontal lobotomy.[4]

To date, a record has been taken from each subject every three to four months subsequent to the operation. Fifteen patients had electroencephalographic recordings only after the cerebral injury (operation). For the latter group the elapsed time from operation to recording ranged from one month to six years.

All tracings were made with a Grass three channel electroencephalograph.

RESULTS

The anatomic existence of a primary focal lesion was obvious from the nature of the operation.[3] However, that the electrical pathophysiologic response was also focal had to be demon-

4. Prefrontal lobotomy in the patients under consideration was performed by Watts and Freeman (J. Internat. Coll. Surgeons **5**:233-240 [May-June] 1942), through burr holes in the coronal suture. The cortex was punctured in an avascular area close to the junction of Brodmann areas 9, 44, 45 and 46, and the subcortical white matter was severed rather completely in the plans of the coronal suture. This separated the frontal pole, comprising areas 9, 10 and 46 on the lateral surface and area 32 on the mesial surface, from the rest of the brain. The incisions seldom went down so far as to undercut areas 10, 11 and 12, at the base of the frontol lobe, or up so far as to affect area 8 to any notable degree. The surgeon attempted to avoid injury to the cortex both to prevent bleeding and to diminish likelihood of subsequent epileptic seizures.

In several of the cases reported here, secondary operations were performed through burr holes placed 3 cm. from the midline and 1 to 1.5 cm. behind the coronal suture, the subcortical incisions being made close to the junction between areas 6 and 8. Freeman and Watts (personal communication to the author) have observed a high incidence of epileptic seizures in patients undergoing secondary operations.—Walter Freeman.

strated. This was accomplished, as shown in figure 1. In this recording electrodes were radially arranged in four straight rows around one burr hole. The first electrode in each row was placed ½ inch (1.27 cm.) from the margin of the defect in the skull. Each succeeding electrode was separated 1 inch (2.5 cm.) from its predecessor. All leads were taken with respect to the right ear. It was observed that the greatest number of high voltage slow waves were in the most rostral parasagittal leads; as one proceeded caudally and paracoronally, the prominence of the low frequency activity decreased. Hence it was established that the "immediate" abnormal electroencephalographic response to prefrontal lobotomy was focal (frontal), in conformity with the anatomic lesion.

In all subjects from whom records were taken within ten days after operation, high voltage slow wave discharges were observed in the symmetric frontal leads (fig. 2). The frequency ranged from 2 to 4 waves per second. In this same group, usually within one to three months after operation, the prominent low frequency oscillations were replaced with short sequences of 6 per second waves of reduced amplitude. In most subjects this low intensity abnormality persisted as a subdominant characteristic as long as

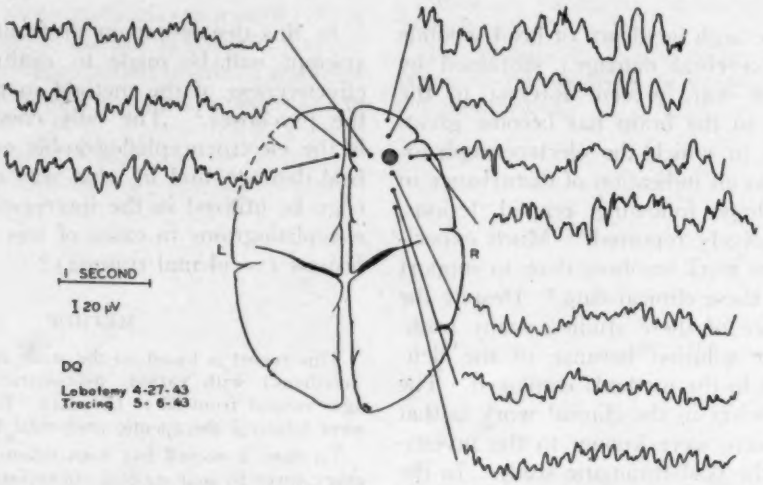

Fig. 1.—Focal electroencephalographic response to focal injury to the brain. The maximum abnormality is in the most rostral leads.

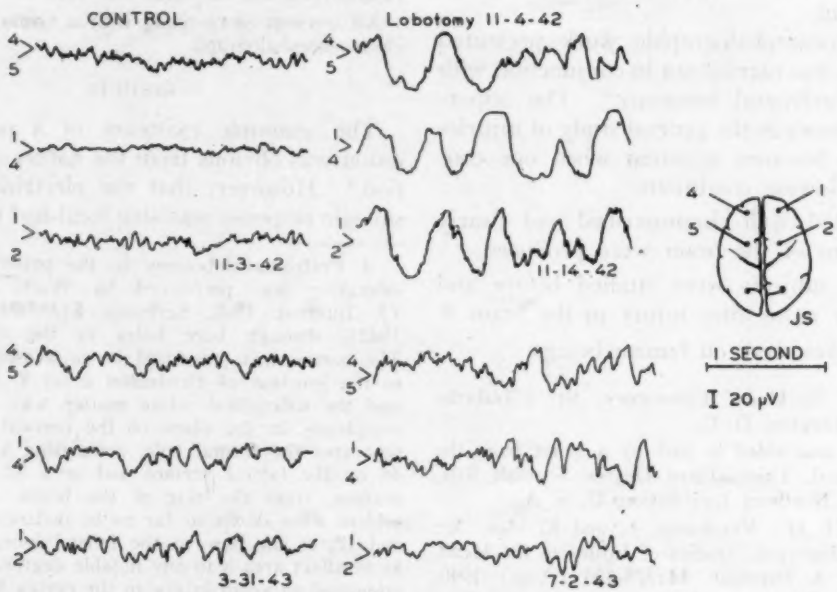

Fig. 2.—Typical electroencephalogram after prefrontal lobotomy. Moderate slow wave activity usually persists in the region of structural damage.

recordings were made. The variations in parietal and occipital potentials maintained their preoperative frequency, but usually developed greater prominence (higher voltage) after operation.

In 3 subjects from whom recordings were obtained with frontal leads within a month after operation no evidence of abnormal wave forms

Certain subjects (fig. 4) who within a relatively short time after operation showed only medium voltage slow waves, primarily in transverse leads, later exhibited prominent and persistent high voltage, approximately 4 per second waves in all frontal derivations.

For 1 subject (fig. 5) from whom no preoperative records were obtained, a postoperative

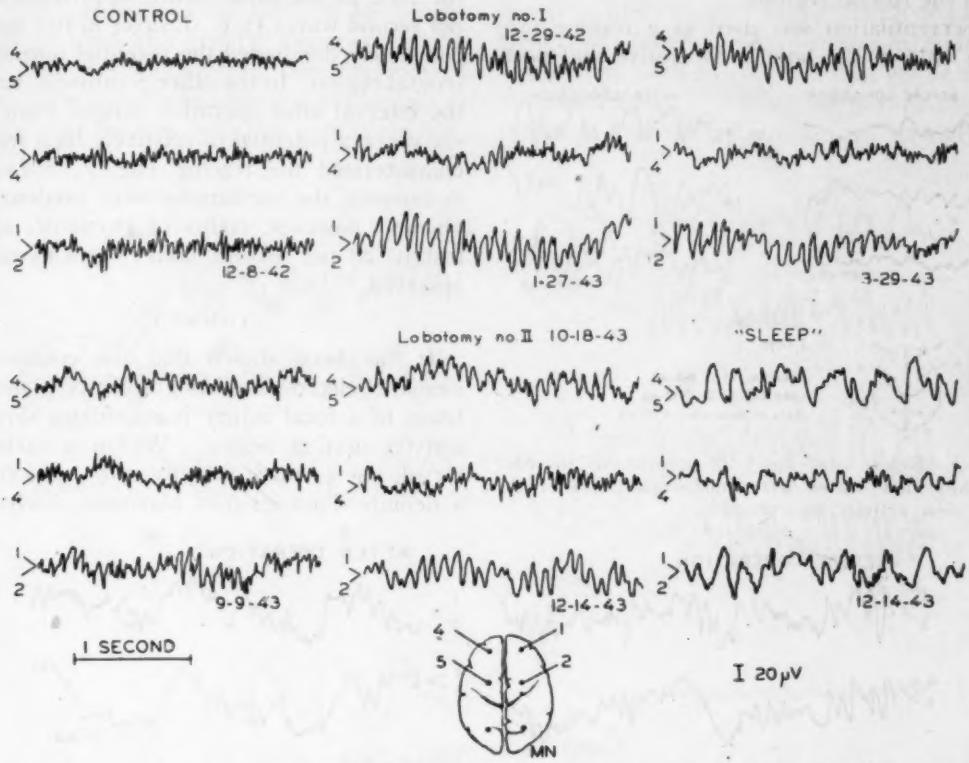

Fig. 3.—Enhancement of alpha activity following prefrontal lobotomy. Slow wave discharges during "sleep" are observed in the tracings in the lower right portion of the figure.

was recognized. Figure 3 shows portions of the electroencephalogram of 1 of these patients. It was seen that the preoperative high frequency pattern was replaced after the operation by entirely normal-appearing alpha waves. About nine months later, however, there was a regression to the high frequency pattern of the control type. A second lobotomy, ten months after the first, again failed to produce any abnormal electric response. This phenomenon of no demonstrable change in the electroencephalogram following injury to the brain raised the question whether slow wave activity could develop in such a brain. That no delta wave–inhibiting mechanism was active in this particular subject at least was beautifully shown in the low frequency discharges associated with moderately deep "spontaneous" sleep (group of waves in lower right portion of figure).

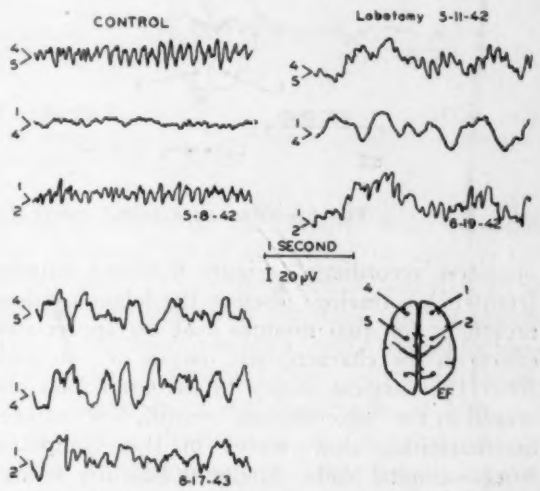

Fig. 4.—Moderately abnormal electroencephalogram five weeks after lobotomy (most prominent in the transverse frontal lead). Slow wave discharges dominated the output of potential approximately one year after operation.

tracing (one month after the second lobotomy) showed some slow discharges in the frontal leads, ranging in duration from one hundred and sixty to two hundred and fifty milliseconds. Nearly five months after the electroencephalographic recording he had a clinical epileptic seizure. An electroencephalogram taken six weeks after the convulsion showed a dominant delta wave pattern in the frontal regions.

Hyperventilation was used as a routine procedure only in the later preoperative and post-

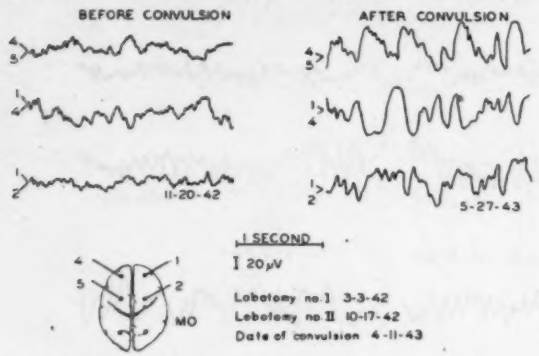

Fig. 5.—Before the onset of convulsive disorder abnormally slow waves were subdominant. After the seizure slow activity was prominent.

Of the 15 patients from whom no preoperative records were taken, it was observed that 10 showed pronounced electroencephalographic abnormalities even four to six years after injury to the brain (operation). Patient EC (fig. 7) clearly presented generalized abnormality in the electroencephalogram, with the maximum abnormality in the right frontal area. In the record for AH, in the same figure, approximately 1½ per second waves (i. e., 3 waves in two seconds), completely dominated the potential output of the frontal region. In the other 5 subjects, for whom the interval after operation ranged from two to six years, a potential of relatively high frequency characterized the tracing (fig. 7, *EA*). Predominantly the oscillations were random in frequency; however, trains of rhythmic, approximately 20 per second waves were occasionally observed.

COMMENT

It has been shown that the common "immediate" electroencephalographic response of the brain to a focal injury is maximum slow wave activity in that region. Within a variable interval, one to three months, most subjects show a definite diminution of abnormal discharges of

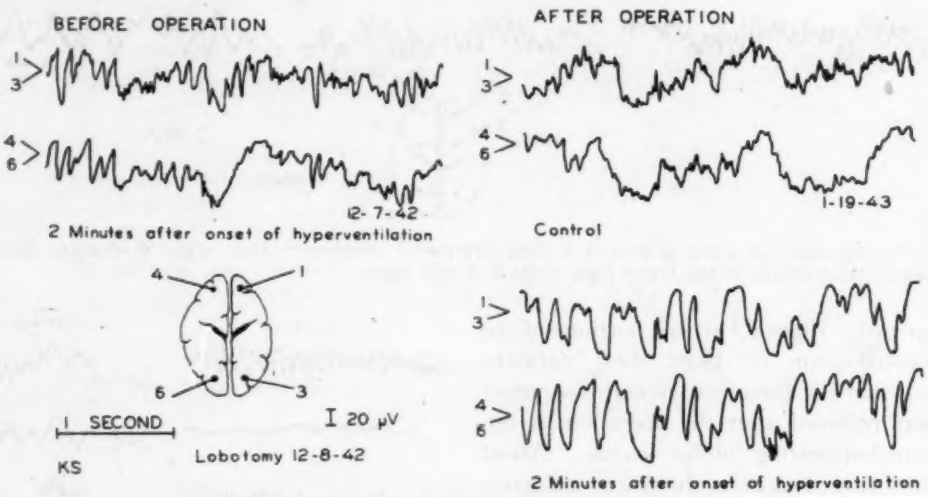

Fig. 6.—Effect of cerebral injury (operation) on response to hyperventilation.

operative recordings. Figure 6 shows samples from such a tracing. Before the lobotomy deep breathing for two minutes had no appreciable effect on the characteristic output of potential. After the surgical injury to the brain one observed in the "spontaneous" record, low voltage, nonsinusoidal, slow waves in the symmetric fronto-occipital leads. Moderate base line swinging was also seen in the control pattern. Two minutes after the onset of overventilation prominent sequences of delta waves dominated the record.

potential over the damaged area of the brain. Furthermore, for the lobotomized patient it has been shown that in the presence of minimal abnormal activity in the "spontaneous" record hyperventilation greatly accentuates the low frequency characteristic of the electroencephalogram. These results conform to and confirm, in all essentials, the electroencephalographic findings in the record of the majority of patients with acute head injuries.

Before the true import of prefrontal lobotomy as an experiment in controlled injury

to the brain was recognized, it was difficult to evaluate properly the marked focal or general abnormalities in the records of patients with a history of old head trauma. The question always arose as to whether the electroencephalographic abnormality was a direct result of the cerebral insult or an expression of a pretraumatic physiologic (epileptoid) disturbance. As is evident in the work presented, old cerebral lesions do give rise to focal and general electroencephalographic changes; consequently, the presence of prominent electroencephalographic abnormalities with old head injuries must be considered primarily as causally related to the cerebral damage unless pretraumatic tracings were made.

A further important fact pertaining to brain injury emerged from the studies on prefrontal lobotomy, namely, that even in the presence of known cerebral damage (acute and chronic) electroencephalographic abnormalities may be minimal or absent. As shown in figure 3, certain normal characteristics may actually be enhanced after injury to the brain.

The electroencephalographic phenomenon seen in the case of MO (fig. 5) was earlier observed by me in 2 cases of bullet wounds of the brain. In each instance pronounced slow activity did not appear until after the onset of a clinical convulsive disorder. If one allows the assumption that the slow waves came on concomitantly with or just previous to the seizure, then the hypothesis of Gibbs, Gibbs and Lennox [5] that cerebral dysrhythmia is the cause of the epilepsies appears to be confirmed. The absence of any seizures in other subjects with pronounced focal and general electroencephalographic abnormalities, such as AH and EC, whose records appear in figure 7, EF whose records appear in figure 4, and others not shown, strongly indicates, however, that the cerebral dysrhythmia is not the cause, but is one factor (or sign) in the development of convulsive states, and that an ill defined constellation of variables, not yet clearly recognized, must interact in order to give expression to the syndrome of the clinical epilepsies.

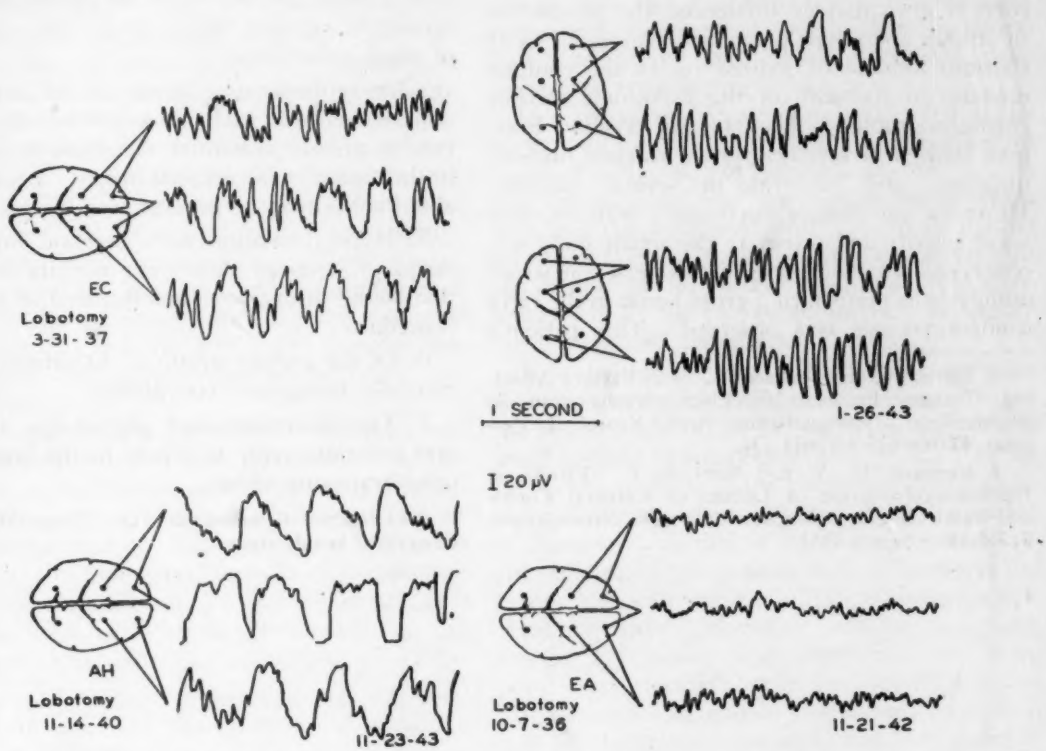

Fig. 7.—*EC*, electroencephalogram showing generalized abnormality nearly six years after operation; *AH*, prominent slow wave activity three years after operation (all possibility of artefact potentials has been carefully excluded); *EA*, random high frequency oscillations six years after cerebral damage.

In recent years the importance of hypoglycemia for the development of slow wave activity during hyperventilation has been heavily empha-

5. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Epilepsy: Paroxysmal Dysrhythmia, Brain **60**:377-388 (Dec.) 1937. Lennox, W. G.: The Drug Therapy of Epilepsy, J. A. M. A. **114**:1347-1356 (April 6) 1940.

sized.[6] The results shown in figure 6 forcefully bring out the fact that injury to the brain (neuronal disturbance) is an important factor in the production of slow waves during the process of deep breathing. This clear finding thus makes it necessary partially to deemphasize the role of blood sugar in the production of slow waves during overventilation and to weigh the relative importance of neuronal damage and elementary metabolic disturbances in each individual case under study.

The persistent low frequency activity observed as a late phenomenon of prefrontal lobotomy raised the question whether damage of subcortical gray masses influenced the production of these abnormal potential changes.[7] With thorium dioxide or iodized oil as the contrast medium in the path of the leukotome section, roentgenographic studies by Dr. Walter Freeman showed involvement of the caudate nucleus, unilateral and bilateral, in several subjects. However, no definite correlation between slow wave activity and injury to the striate body was observed. In the 1 case of this series in which autopsy was performed a gross lesion in the right caudate nucleus was observed. This patient's tracing was characterized by a random high frequency pattern and showed no focal or general slow wave discharges.

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7. Kennard, M. A., and Nims, L. F.: Effects on Electroencephalogram of Lesions of Cerebral Cortex and Basal Ganglia in Macaca Mulatta, J. Neurophysiol. **5**:335-348 (Sept.) 1942.

CONCLUSIONS AND SUMMARY

1. The primary electroencephalographic response of the human brain to localized injury (prefrontal lobotomy) is the production of focal slow waves. These may or may not persist.

2. With lobotomized patients the return of the electroencephalographic pattern to a relatively normal pattern usually requires one to three months.

3. Certain persons show no demonstrable response to cerebral injury under the conditions of these experiments.

4. A representative group of subjects show apparent normal early recovery and then again exhibit grossly abnormal variations in potential in the region of the original injury. At times the abnormality may be general.

5. Hyperventilation after cerebral injury induces pronounced slow wave activity in brains that before injury were uninfluenced by a similar procedure.

6. Of the present group of 30 patients, 1 had clinically recognized convulsions.

7. The aforementioned phenomena are general and thus apply to injury to the brain from other traumatic agents.

Dr. Walter Freeman and Dr. James W. Watts cooperated in this study.

TRANSTENTORIAL HERNIATION OF THE BRAIN STEM

A CHARACTERISTIC CLINICOPATHOLOGIC SYNDROME; PATHOGENESIS OF HEMORRHAGES IN THE BRAIN STEM

I. MARK SCHEINKER, M.D.
CINCINNATI

While death due to medullary compression associated with herniation of the cerebellar tonsils has long been known, relatively little attention has been paid to the sequela of compression of the brain stem caused by herniation of the stem through the tentorial opening. In 1920 Meyer called attention to medial displacement and herniation of the hippocampal gyrus into the tentorial incisura in cases of space-consuming intracranial lesions. The subject was later elaborated by van Gehuchten,[1] Jefferson,[2] Reid and Cone,[3] Moore and Stern [4] and Smyth and Henderson.[5] All these contributors have amply demonstrated that space-consuming lesions may cause appreciable herniation of the hippocampal gyrus of the temporal lobe into the potential space that lies directly above and between the free edges of the tentorium cerebelli and the brain stem.

The same type of herniation has been recently observed by Schwarz and Rosner [6] in 100 cases of supratentorial space-consuming lesions. The clinicopathologic relations were studied in 43 selected cases. These authors frequently observed the following signs and symptoms: fluctuation in the state of consciousness; anisocoria, with or without dysfunction of the pupillary light reflexes; imbalance of extraocular muscles; cardiorespiratory and thermoregulatory disturbances; paradoxic and shifting signs of involvement of the pyramidal tracts; decerebrate rigidity, and stiffness of the neck. These signs and symptoms occurred irregularly and were exaggerated by lumbar puncture, encephalographic and ventriculographic procedures or craniotomy.

In a recent study [7] attention was called to the occurrence of the same type of herniation in cases of epidural and subdural hematoma. It was demonstrated that the shift of the temporal lobe and the associated hippocampal herniation were not the result solely of the space-consuming action of the hemorrhage but were contributed to by the edematous increase in bulk of the traumatized cerebral hemisphere.

It is the purpose of this study to demonstrate that the gravity of the clinical syndrome is not the result solely of the herniation of a relatively small portion of compressible tissue, such as the hippocampal gyrus of the temporal lobe; a much more important element is the frank herniation of the rostral portion of the brain stem through the tentorial opening, associated with edema and hemorrhages in the midbrain. This pathologic condition should therefore not be designated merely as "hippocampal herniation" or "temporal pressure cone" but, rather, should be called "transtentorial herniation of the brain stem." It will be shown that transtentorial herniation of the brain stem occurs with different types of cerebral lesions, irrespective of their cause, and that it is accompanied by the development of severe edema and hemorrhage in the brain stem. The character and severity of the lesions in the midbrain, as well as their distribution, are influenced primarily by the degree of compression of the larger veins of the brain stem and the extent of interference with venous outflow.

It is the hope that this pathologic study will furnish a broader basis for a clinical and physiologic approach to the problems involved.

From the Laboratory of Neuropathology, Cincinnati General Hospital, and the University of Cincinnati College of Medicine.

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MATERIALS AND METHODS

This report is based on the study of 55 cases of transtentorial herniation of the brain stem, which may be classified under the following heads:

A. Cerebral vascular disease
   1. Massive cerebral hemorrhage
      (*a*) In association with arterial hypertension
      (*b*) In association with cerebral arteriosclerosis
   2. Cerebral softening due to vascular occlusion in association with cerebral arteriosclerosis

B. Trauma

C. Space-consuming lesions
   1. Brain tumor
   2. Brain abscess

PROTOCOLS

A. CEREBRAL VASCULAR DISEASE

MASSIVE CEREBRAL HEMORRHAGE DUE TO ARTERIAL HYPERTENSION

CASE 1.—A. T., a woman aged 48, was first admitted to the hospital on Jan. 8, 1943 with a history of severe pain in the left eye and gradual loss of vision. Examination gave normal results except for advanced hypertensive retinopathy. The blood pressure was 200 systolic and 120 diastolic.

The patient was readmitted to the hospital on April 14, 1943, in profound coma. The blood pressure was 225 systolic and 140 diastolic. The right pupil was dilated and reacted slowly to light. Advanced papilledema in the right eye was associated with numerous retinal hemorrhages.

Spinal puncture disclosed an initial pressure of 550 mm. of water. The fluid was grossly bloody. The patient died on the day of admission.

Necropsy revealed myocardial hypertrophy and cardiac dilatation associated with arteriolar nephrosclerosis.

Examination of the brain showed fulness of the right hemisphere, especially evident in the right temporal lobe. There was a well defined indentation in the herniated and swollen uncus on the right side, and the brain stem was shifted to the left.

Coronal sections through the cerebrum revealed massive intracerebral hemorrhage in the right cerebral hemisphere, with rupture into the ventricular system. Figure 1 demonstrates the hemorrhage and the pronounced swelling of the right hemisphere and the right half of the brain stem, associated with shift of the midline structures downward and to the left. There were scattered areas of small hemorrhages in the brain stem and the pons. The right half of the brain stem appeared softened and swollen (fig. 1).

Histologic examination disclosed vascular lesions typical of hypertensive encephalopathy and pronounced thickening and hyalinization of the arterioles and capillaries, with narrowing or obliteration of their lumens. Van Gieson preparations showed proliferation of the pericapillary connective tissue fibrils.

In the gray and white substance of both hemispheres were diffusely scattered foci of tissue disintegration, which consisted of small areas of rarefaction and softening associated with a slight degree of glia cell proliferation. In some areas there was to be seen a more extensive and severe form of destruction, associated with formation of small areas of cystic softening. The majority of these foci suggested a perivascular distribution.

Sections taken from the scattered small hemorrhagic areas of the brain stem and pons showed coalescent, small hemorrhages, most of which disclosed clearly their relation to tremendously congested veins (fig. 2). The vessel wall revealed all degrees of disintegration; in some of the perivenous hemorrhages only the shadow of the wall was to be seen in the center. In the vicinity of almost all the hemorrhages the tremendously engorged veins were surrounded by large masses of extravasated red blood cells, extending into the distended perivascular spaces.

The nerve parenchyma showed a high degree of rarefaction and edema, especially pronounced in the vicinity of the hemorrhages. There was no glial or mesodermal reaction to be seen in the areas of hemorrhage.

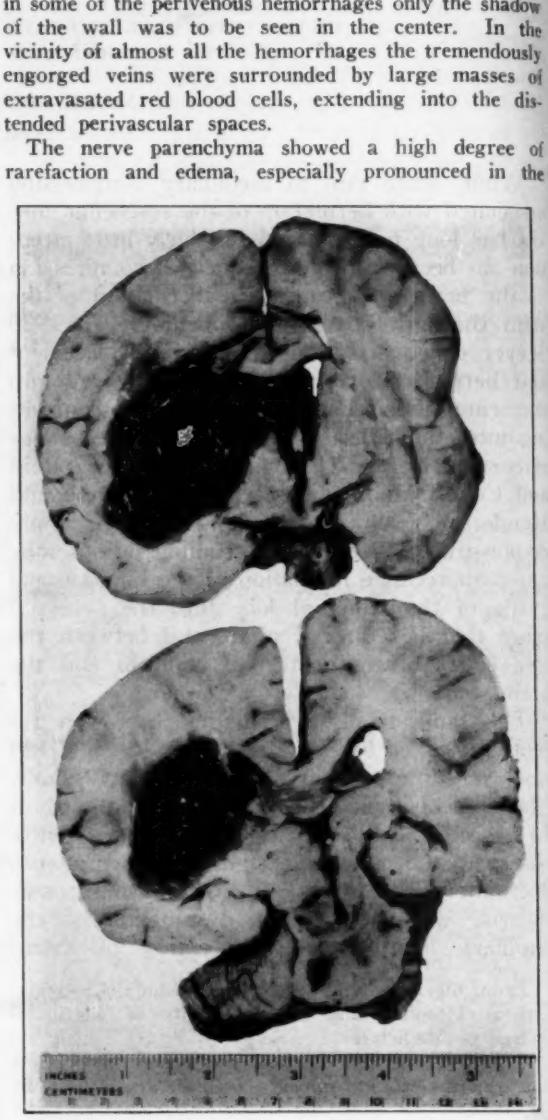

Fig. 1 (case 1).—Massive intracerebral hemorrhage with pronounced swelling of the right hemisphere. Note the swelling and softening of the right half of the brain stem, with shift of the midline structures downward and to the left, and scattered areas of small hemorrhages in the brain stem and pons.

MASSIVE CEREBRAL HEMORRHAGES ASSOCIATED WITH CEREBRAL ARTERIOSCLEROSIS

CASE 2.—M. S., a white woman aged 72, was admitted to the hospital in coma. She was apparently in good health until two weeks before admission, when she acquired a cold. On the day of entrance to the

hospital she was found lying on the floor, unconscious. Examination on admission showed equally dilated, fixed pupils, gasping respiration and an enlarged heart. The systolic blood pressure was 56 mm.; the diastolic pressure was not measurable. The patient died three hours after admission to the hospital.

Necropsy revealed arteriosclerosis, with coronary and aortic atherosclerosis, focal fibrosis of the myocardium and acute cardiac dilatation.

Examination of the brain revealed prominence and fulness of the right parietal lobe. The inferior surface showed a striking fulness of the right temporo-occipital region and shift of the optic chiasm and peduncles to the left. There was a broad uncal herniation on the right side, measuring 2 cm. in length and 1 cm. in width. Coronal sections through the hemispheres revealed an extensive hemorrhage, involving chiefly the right temporoparietal region and extending into the lateral portion of the basal ganglia. There was a striking shift and compression of the ventricular system (fig. 3). The brain stem was distorted, and the aqueduct was displaced sharply to the left. The right half of the brain stem was swollen, and its appearance suggested an early stage of softening. The central portion showed a grayish black discoloration, and numerous small hemorrhages were present.

Microscopic examination revealed far advanced arteriosclerosis. The right half of the midbrain presented swelling and tissue rarefaction. The corresponding half of the brain stem showed loss of myelin sheaths (fig. 4) and the presence of diffusely scattered, numerous petechial hemorrhages, localized chiefly about tremendously congested small veins; the most lateral portion of the left peduncle showed a small area of necrosis (fig. 4), probably due to mechanical compression (Kernohan's notch).

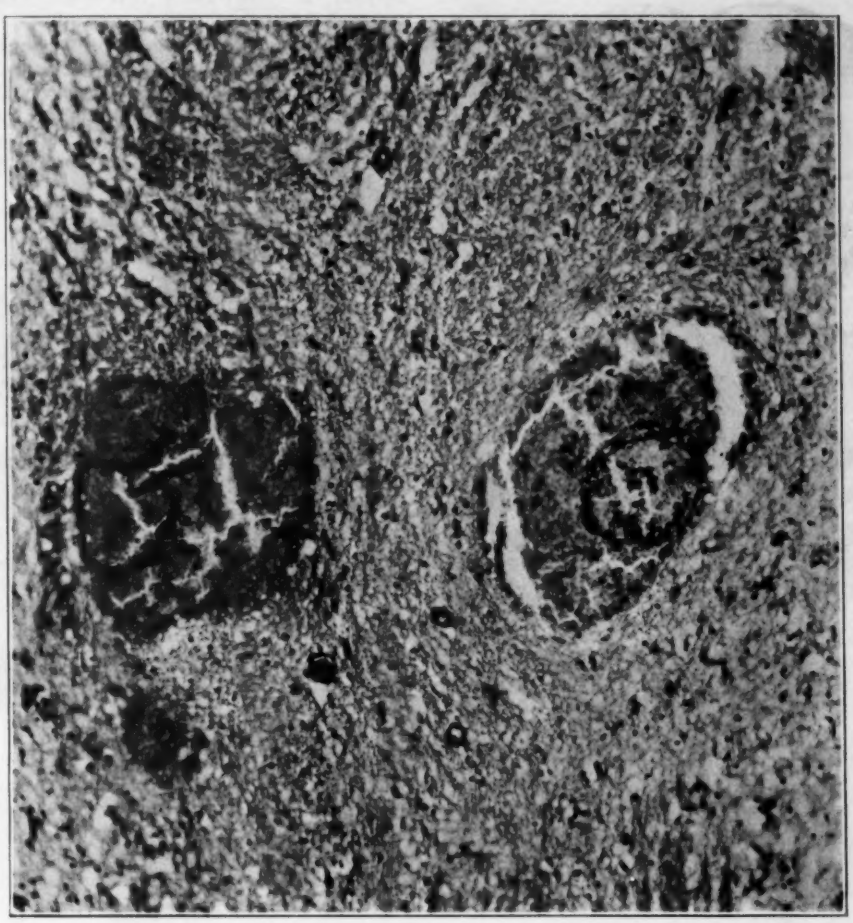

Fig. 2 (case 1).—Perivenous hemorrhage in the brain stem. Note the venous congestion and the disintegration of vessel walls. Hematoxylin-eosin stain; × 125.

CEREBRAL SOFTENING DUE TO VASCULAR OCCLUSION IN CASES OF CEREBRAL ARTERIOSCLEROSIS

CASE 3.—M. B., an obese woman aged 60, was admitted to the hospital because of paralysis of her left extremities, which had developed two hours previously. Examination on admission revealed a stuporous, semicomatose condition and Cheyne-Stokes respiration. The pupils were small, equal and slightly irregular and did not react to light. There were bilateral ptosis and flaccid paralysis of the upper and lower extremities on the left side.

The cerebrospinal fluid was slightly xanthochromic, with an initial pressure of 200 mm. of water. It contained 361 red blood cells per cubic millimeter and 29 mg. of protein per hundred cubic centimeters. The Wassermann reaction was negative. The patient died two days after admission.

Necropsy revealed pulmonary edema, toxic myocardosis and cardiac hypertrophy and dilatation.

Examination of the brain disclosed a tremendous fulness of the right frontoparietal region, with evidence of softening. Inspection of the under surfaces of the brain revealed a sharp shift of the peduncles to the left, with displacement of the corpora mamillaria. The right middle cerebral artery was occluded by a thrombus, adherent to the vessel wall.

Coronal sections through the hemispheres revealed infarction of the right hemisphere in the area of distribution of the right middle cerebral artery. The entire right hemisphere was swollen and soft to touch. The right lateral ventricle was obliterated (fig. 5). There were numerous small hemorrhages in the peri-

Fig. 3 (case 2).—Extensive massive hemorrhage involving the right temporoparietal region and the lateral portion of the right basal ganglia. Note the extreme swelling of the right hemisphere, associated with shift and compression of the ventricular system, and the swelling and hemorrhagic softening of the right half of the brain stem, with displacement and compression of the aqueduct of Sylvius.

aqueductal region and in the lateral portion of the left superior colliculus. The right half of the midbrain appeared broader and was somewhat soft to touch. In the pons extensive hemorrhage involved the crossing fibers and extended dorsally into the right brachium pontis.

Microscopic examination of the brain stem and pons disclosed edema and congestion. There were small hemorrhages, which, with few exceptions, were present about tremendously congested veins, the walls of which had undergone almost complete disintegration. Near the periphery of the hemorrhages were numerous congested veins and capillaries. The perivascular spaces were distended with extravasated blood and serous fluid.

B. TRAUMA

Case 4.—W. R., a man aged 56, sustained a slight laceration of the scalp when struck on the head by the hook of a traveling crane, in May 1938. Subsequently, headache of increasing intensity developed. On the morning of Aug. 24, 1938 he was admitted to the hospital, at which time neurologic examination was reported to reveal nothing significant. That afternoon, however, he became comatose. Examination then showed small, fixed pupils and rigidity of the extremities, which was more pronounced on the right side. Lumbar puncture revealed an initial pressure of 260 mm. of water. The coma deepened. Burr openings placed bilaterally in the occipital area revealed a subdural

Fig. 4 (case 2).—Loss of myelin sheaths in the swollen half of the brain stem. Note the downward displacement and compression of the left peduncular region, and the small area of necrosis, probably due to mechanical compression (Kernohan's notch) in the lateral portion of the left peduncle. Loyez stain for myelin sheaths.

hematoma on the left side, and about 50 cc. of a reddish brown fluid was released, under considerable pressure. Consciousness was not regained. The patient died on the morning of August 25.

The pertinent lesions in the brain are illustrated in figure 6. There was fulness of the entire left hemisphere. This was especially pronounced in the temporal and occipital lobes because of the presence of hemorrhagic infarction in the distribution of the left posterior cerebral artery. There resulted compression of the left lateral ventricle and shift of the midline structures to the right. Figure 6 *B* illustrates the hemorrhages in the midbrain and pons.

Microscopic examination of the brain stem revealed changes similar to those described in the preceding cases.

C. SPACE-CONSUMING LESIONS

BRAIN TUMOR

CASE 5.—C. B., a man aged 44, had been well until the day of admission, when he began to talk incoherently and became disoriented.

Examination revealed inequality of the pupils, which reacted briskly to light; slight right hemiparesis, and a positive Babinski sign bilaterally.

The cerebrospinal fluid was slightly xanthochromic and was under a pressure of 200 mm. of water; it contained 20 lymphocytes and 60 red blood cells per cubic millimeter and 600 mg. of protein per hundred cubic centimeters. The Wassermann reaction was negative. The patient died thirteen hours after admission.

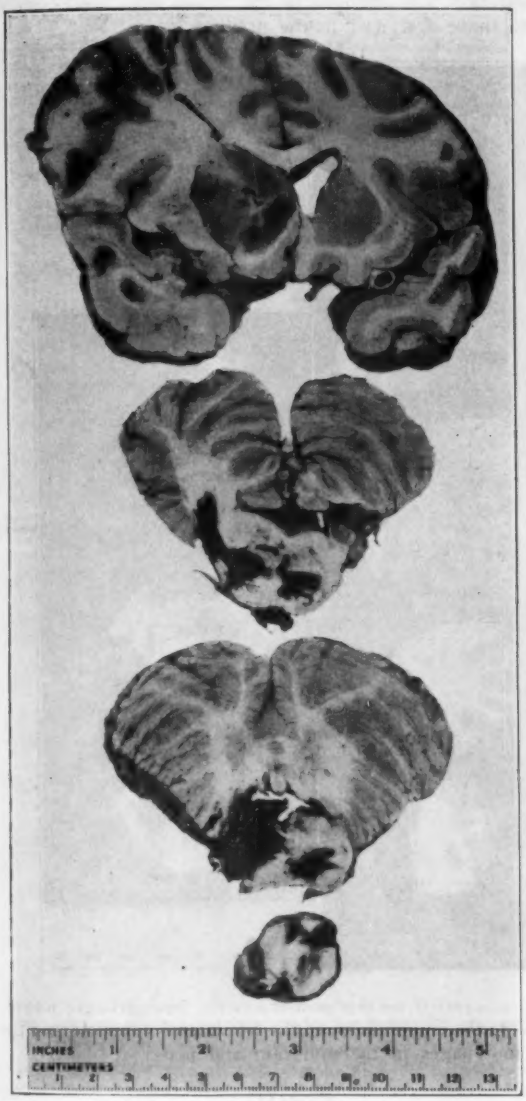

Fig. 5 (case 3).—Infarction of the right hemisphere in the area of distribution of the right middle cerebral artery. Note the tremendous swelling of the entire right hemisphere, with obliteration of the right lateral ventricle, and multiple hemorrhages of the brain stem.

The significant lesions of the brain are illustrated in figure 7. The left hemisphere appeared swollen. The lateral face of this hemisphere was partly destroyed by a large area of hemorrhage in the vicinity of a brownish black tumor, measuring approximately 2 cm. in diameter. The under surfaces of the frontal and temporal lobes revealed numerous brownish black, small tumor nodules. The extreme swelling of the left hemisphere resulted in compression of the left lateral ventricle and a pronounced shift of the midline structures to the right. On the left side was a well defined herniation of the uncus. Coronal sections through the midbrain revealed diffusely disseminated, small hemorrhages, especially numerous in the periaqueductal region and below the floor of the fourth ventricle (fig. 7).

Microscopic examination of the tumor revealed melanosarcoma. The histologic lesions in sections of the midbrain were essentially similar to those in the cases already described. Perivenous hemorrhages, congestion and edema were predominant features.

CASE 6.—G. O., a man aged 66, was admitted to the hospital in coma. During the preceding few years he had been treated for hypertension.

Examination disclosed right spastic hemiplegia, with weakness of the left side of the face, slight ptosis of both upper lids and equality of the pupils, both of which reacted normally to light. The fundi were normal. There was moderate stiffness of the neck. The deep reflexes could not be obtained. The Babinski sign was elicited on the right side.

The cerebrospinal fluid was clear, slightly yellow and under a pressure of 250 mm. of water; it contained 1 lymphocyte and 3 red blood cells per cubic millimeter and 188 mg. of protein per hundred cubic centimeters. The Wassermann reaction was negative.

One month later the patient died of pneumonia.

Necropsy revealed hypertensive cardiovascular disease, lobular pneumonia and congestion and toxic changes in the viscera.

Examination of the brain revealed a large, fairly well circumscribed neoplasm, measuring approximately 5 cm. in diameter, which involved the lateral portion of the left parietal lobe. The adjacent tissue immediately contiguous to the tumor was softened. The left temporal lobe showed a striking herniation of the uncus, which had resulted in displacement of the brain stem to the right. Coronal sections through both hemispheres (fig. 8) revealed tremendous swelling of the left hemisphere, with widening of the white matter and an extreme shift of the ventricular system to the right. Sections through the shifted region of the midbrain disclosed the presence of numerous small hemorrhages in the periaqueductal region and in the vicinity of the median raphe (fig. 8).

Microscopic examination of the tumor revealed a glioblastoma multiforme. Sections taken from the white matter of the left hemisphere showed a severe degree of edema and tissue liquefaction. The predominant change in sections from the brain stem consisted of tremendous congestion and engorgement of the large and small veins, associated with numerous coalescent perivenous hemorrhages.

BRAIN ABSCESS

CASE 7.—F. S., a man aged 30, was admitted to the hospital in deep coma. Four weeks prior to admission left hemiparesis developed suddenly. In the few days before his entrance to the hospital he had several focal seizures, confined to the left extremities.

Examination disclosed complete left hemiparesis, a Babinski response bilaterally and Cheyne-Stokes respiration.

The cerebrospinal fluid was clear and colorless and under a pressure of 350 mm. of water and contained 74 lymphocytes and 58 red blood cells per cubic millimeter.

Ventriculograms showed a shift of the ventricular system to the left. A bone flap was turned down in the right parietal region. When the dura was opened, purulent fluid and air were obtained. The fluid contained diplococci. The patient died two hours after operation.

displaced downward and was compressed. The midline structures were shifted to the left. The right thalamus appeared broader than the left. There was a small hemorrhage in the region of the left ansa lenticularis. Examination of the brain stem disclosed diffuse swelling and the presence of a small number of petechial hemorrhages.

Microscopic examination revealed the characteristic features of an abscess surrounded by a broad zone of granulation tissue. Sections taken from the white matter of the right hemisphere showed far advanced edema. The changes in the brain stem were similar to those described in the previous cases.

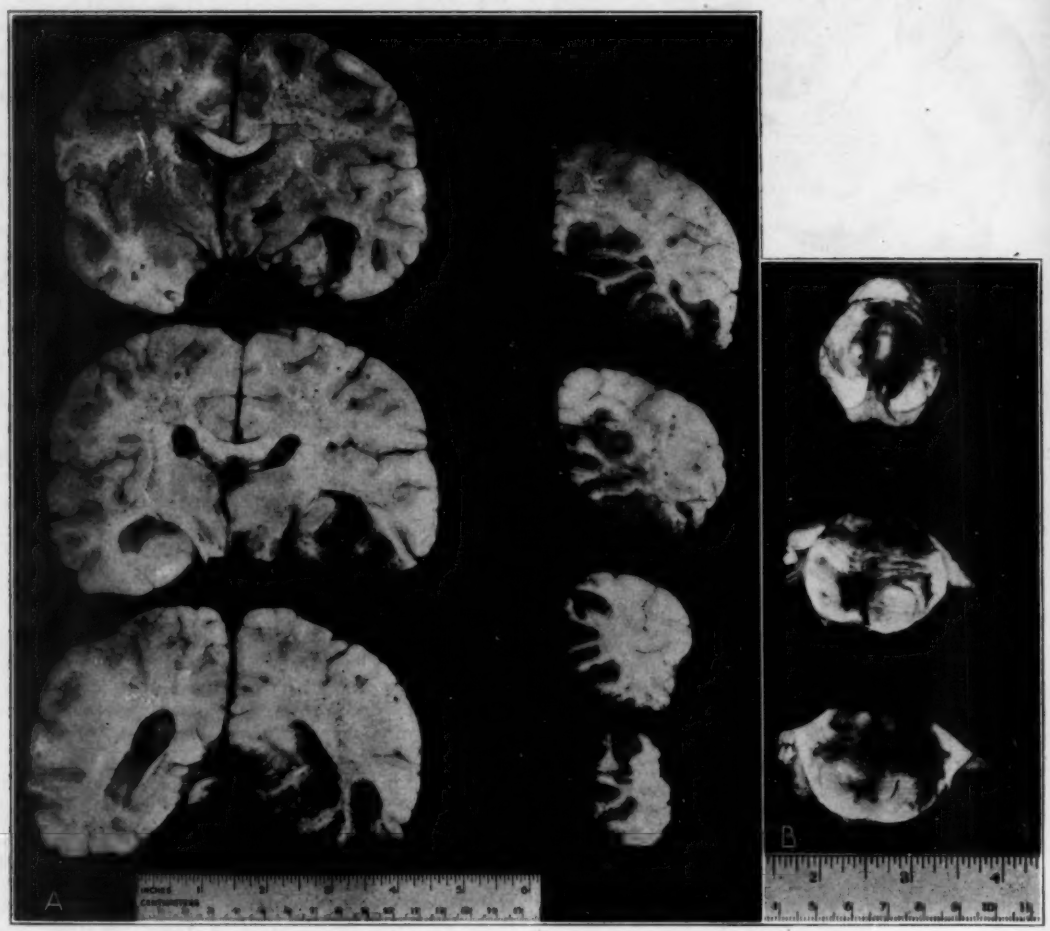

Fig. 6 (case 4).—*A*, fulness of the entire left hemisphere, associated with a post-traumatic hemorrhagic infarction in the distribution of the left posterior cerebral artery. Note the compression of the left lateral ventricle and the shift of the midline structures to the right. *B*, extensive hemorrhages in the midbrain and pons.

The pertinent lesions in the brain are illustrated in figure 9. The right hemisphere showed striking prominence and fulness, with bulging of the precentral and postcentral gyri. This was caused by an abscess. The cavity of the abscess measured 3.3 cm. in its greatest diameter and was surrounded by a broad zone of hyperemia. The right hemisphere showed enormous swelling, which was due chiefly to edematous tissue, involving the white matter in largest part and in some areas almost completely obliterating the gray matter. The right temporal lobe showed a well defined uncal herniation, measuring 2 cm. in length and 8 mm. in width, with a clear indentation from the ipsilateral free edge of the tentorium. The right ventricle was

COMMENT

A number of significant points have emerged from this study.

Frequent Occurrence of Unilateral Cerebral Swelling and Herniation of the Brain Stem Through the Tentorial Opening.—While the mesial displacement and herniation of the hippocampal gyrus is a common observation in cases of brain tumor, as indicated by Jefferson,[2] and in cases of brain injury, as described by Evans and me,[7] its association with massive hemor-

rhages and cerebral infarctions has not been stressed. Careful analysis of the described cases revealed that in addition to the hippocampal herniation there was a frank herniation of the rostral portion of the brain stem through the tentorial opening. In all the cases cited in the present study histologic analysis of the swollen hemisphere disclosed a picture typical of cerebral edema, characterized by distention of perivascular and pericellular spaces, transudation of

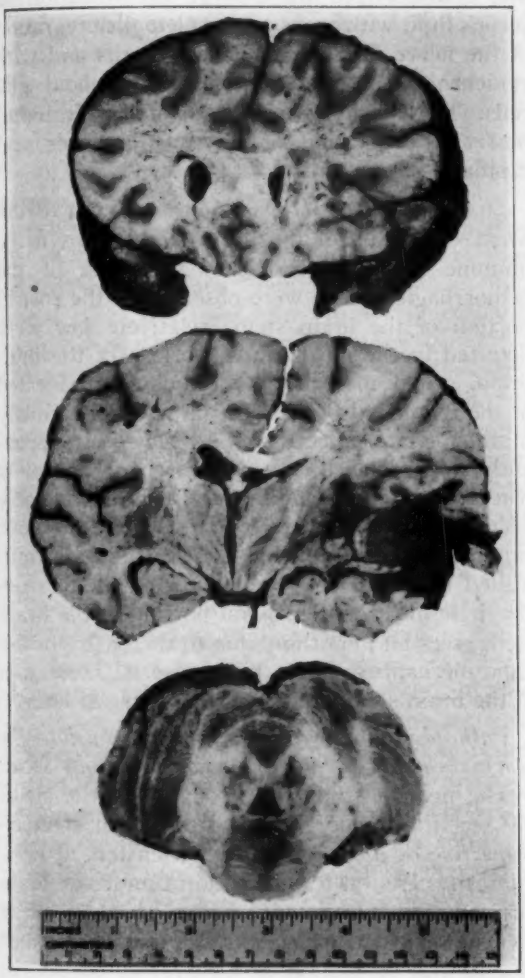

Fig. 7 (case 5).—Melanosarcoma of the left temporoparietal region, with extreme swelling of the left hemisphere and compression and shift of the ventricular system. Note the diffusely disseminated hemorrhages in the brain stem.

serum into the nerve tissue about the congested smaller blood vessels, distention of perineural spaces and an alveolar, sievelike appearance of the nerve parenchyma. The significant role of edema in the production of the herniation of the temporal uncus over the free edge of the tentorium has been emphasized in a previous paper.[7] The mechanism of the shift and compression of the ventricular system is readily explained by the unilateral swelling of the brain, sufficient in some instances even to cause displacement of the affected hemisphere across the midline under the free edge of the rigid falx. Inasmuch as the falx in the adult is a relatively immobile structure, it is obvious that there must be a tendency toward displacement of the swollen hemisphere beneath the free edge of the falx, causing herniation of the supracallosal gyrus.

In the instances of more severe edema the same side of the brain stem was observed to be swollen. Of still greater significance was the regularly observed herniation of the rostral portion of the midbrain through the tentorial opening. It is evident that as a result of the swelling of the cerebral hemisphere the mesial portion of the temporal lobe lying immediately

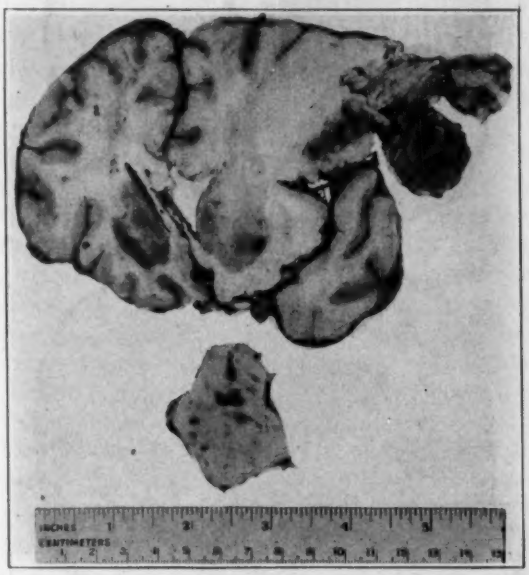

Fig. 8 (case 6).—Glioblastoma of the left parietal region, with extreme swelling of the left hemisphere and displacement of the ventricles to the right. Note the presence of numerous periaqueductal hemorrhages in the brain stem.

above the incisura tentorii was the first to be displaced downward through this incisure. With increase in the duration and severity of the edema, downward displacement and frank herniation, with distortion and compression, of the rostral portion of the midbrain take place.

Origin and Pathogenesis of Hemorrhages of the Brain Stem.—In the literature stress is laid on the arterial origin of the hemorrhages in the brain stem (Moore and Stern[4] and others). The present study indicates that they are related to the medium-sized and small veins. They were often noted in the form of narrow bands enclosing the congested veins like a sleeve, either occu-

pying the perivascular spaces or lying free in the adjacent nerve tissue. In many instances the smaller hemorrhages tended to fuse and in this way gave rise to larger hemorrhages. Only in relatively few instances, in which the hemorrhagic lesions were more extensive, was it difficult, or impossible, to be sure of the source of the hemorrhage; this was mainly because of complete disintegration of the tissue and abundance of blood. Within the large majority of the smaller hemorrhagic lesions there were recog-

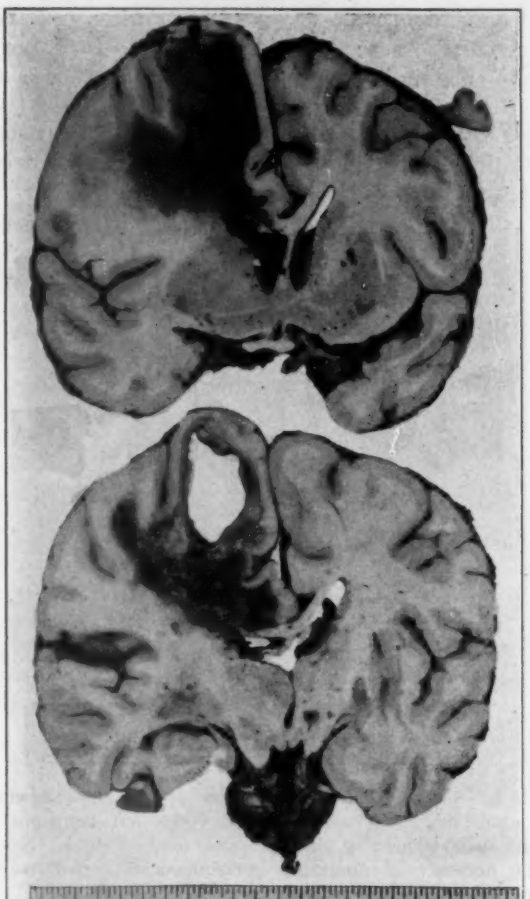

Fig. 9 (case 7).—Large abscess of the right centroparietal region, associated with swelling of the right hemisphere. Note the downward displacement of the right peduncular region and a small hemorrhage in the region of the left red nucleus.

nized as a rule one or several tremendously congested veins, with walls displaying advanced disorganization but not real rupture. In some instances the veins were represented by a mere outline of the wall (fig. 2). The latter had undergone almost complete degeneration, and the content of the vein merged with the extravasated blood surrounding the vessel. The perivascular spaces were maximally distended and filled with large masses of serous fluid and red blood cells.

Extrahemorrhagic Changes in Nerve Tissue of the Brain Stem.—The hemorrhages in the brain stem were, with few exceptions, outlined with extremely edematous tissue. This tissue was characterized by a cribriform, spongy appearance, with the formation of a large number of vacuoles, of different sizes and shapes. In some areas there was extreme liquefaction of the nerve parenchyma, characterized by a large accumulation of serous fluid with areas of complete disintegration of the nerve fibers and myelin sheaths and with evidence of degeneration of the ameboid glia cells. These changes were associated with dilatation and congestion of the smaller veins and capillaries.

Distribution of Hemorrhages in the Brain Stem.—No part of the brain stem seems to be immune from hemorrhage. Yet most of the hemorrhagic lesions were observed in the rostral portion of the brain stem; relatively few were detected in the most caudal portion of the midbrain. The majority of lesions were located in the tegmental portion of the midbrain, chiefly in the periaqueductal region. There is apparently a predisposition to hemorrhage at points where the loose texture of the extremely edematous gray matter forms a relatively poor support for the tremendously congested, thin-walled veins. This predilection of the hemorrhagic lesions for the rostral portion of the brain stem gives an important clue to the pathophysiologic mechanism of the transtentorial herniation of the brain stem which will be discussed later.

Pathophysiologic Mechanism Responsible for Herniation and Hemorrhages of the Brain Stem.—The present study has brought out the striking fact that hemorrhages of the brain stem irrespective of their origin—hypertension, arteriosclerosis, cerebral trauma, brain tumors or brain abscess—are associated with cerebral swelling and subsequent displacement of the ventricular system and herniation of the rostral portion of the mesencephalon through the incisura tentorii. The following theory of the mechanism responsible for the development of edema and hemorrhage in the brain stem is proposed for consideration: The observations recorded in this study afford evidence that a sudden increase in bulk of one of the cerebral hemispheres caused by acute edema or swelling of the brain leads to an acute increase in the supratentorial pressure. In the earlier stages the affected cerebral hemisphere displaces cerebrospinal fluid from the subarachnoidal space and from the cisterns. At a later stage the ever-increasing demand for space leads

to profound shifts of cerebral substance; the initial formation of a temporal pressure cone is followed by downward displacement and herniation of the brain stem, with subsequent plugging of the tentorial hiatus, producing a bottleneck for both the subarachnoid and the ventricular fluid. At the same time, the shifting cerebral substance may compress or occlude the narrow aqueduct of Sylvius, and the intraventricular fluid becomes trapped in the lateral and third ventricles. This leads to a steadily progressing disparity between the intracranial pressure above and that below the tentorium. With the constant increase of the intraventricular pressure the herniated portion of the brain stem is pushed deeper into the tentorial opening. As it progresses, it leads to compression and kinking of the superficial blood vessels, especially the veins, with considerable obstruction of the venous circulation and a resultant severe degree of congestion and stasis. The thin-walled, smaller veins, composed of simple endothelial tubes, are most likely to be vulnerable to compression and to anoxemic degenerative changes in their walls due to anoxemia resulting from stasis. Thus, in the earlier stages compression of thin-walled veins between the impinging uncus and the brain stem is believed to occur. In the later stages the possibility of interference with free venous outflow is even greater because the cerebral substance and the intervening veins are jammed against rigid dural reflections. This is believed to result in a severe degree of congestion and stasis, local venous hypoxia, due to the stasis, and possibly degenerative changes in the walls of the veins. Finally, if complete block of cerebrospinal fluid occurs, the smaller veins are ready to give way, and numerous perivenous extravasations take place. The small veins of the periaqueductal region are evidently poorly supported by the loose tissue of the gray substance, as compared with those of the white matter, which explains the predilection of the perivenous hemorrhages for this region. The fixation of a certain number of the larger superficial veins of the brain stem for a long distance parallel to a bony surface makes them more exposed to the increased pressure.

The anatomic observations in support of this theory of mechanism may be listed as follows: (1) the gross and histopathologic evidence of swelling or edema of the brain present in the affected hemisphere; (2) transtentorial herniation of the rostral portion of the brain stem, as observed in all cases reported in this study, and, finally, (3) the predominantly perivenous character of the hemorrhages in the midbrain associated with far advanced venous congestion and stasis.

CLINICAL OBSERVATIONS

In the past the pressure within the cerebral ventricles was considered to be always in equilibrium with the pressure throughout the spinal subarachnoid space. The observations of Hodgson [8] and Smyth and Henderson [5] give strong support to the belief that the lumbar and the ventricular pressure are not of necessity always equal. Hodgson reported a series of 49 cases of intracranial tumor in which he studied the ventricular and lumbar pressures. He concluded that partial block might result from herniation of the cerebellar tonsils and that under such conditions the initial lumbar pressure might be lower than the pressure in the ventricles. The relation between the lumbar and the ventricular cerebrospinal fluid was studied by Smyth and Henderson in a series of 39 patients, the majority of whom had intracranial tumor. Their observations proved that the ventricular pressure exceeded the lumbar pressure in all cases in which the tumor was above the tentorium and in which there was postmortem evidence of herniation of the ipsilateral temporal lobe through the incisura tentorii. On the other hand, in cases in which the tumor was situated subtentorially the lumbar and the ventricular pressure were equal. It is of interest to note that in the last group of cases there was pronounced, and in some cases extreme, tonsillar herniation. On the basis of these extremely interesting and important observations, Smyth and Henderson came to the conclusion that the disparity of the ventricular and the lumbar pressure is due mainly to herniation of the medial border of the temporal lobes into the incisura tentorii, with subsequent compression or obliteration of the iter of Sylvius.

Moore and Stern [4] collected 10 cases of hemorrhages of the brain stem in 130 cases of intracranial tumor. The presence or absence of herniation of the hippocampal gyrus was not stated in every case, but the lesion was present in the majority. In spite of this observation, the authors came to the conclusion that the hemorrhages in the brain stem "are finally brought on by reflex increase in the systemic blood pressure."

EXPERIMENTAL OBSERVATIONS

The relation between the ventricular and lumbar cerebrospinal fluid pressures has recently been studied experimentally by Kahn.[9] An ex-

8. Hodgson, J. S.: The Intracranial Pressure in Health and Disease, A. Research Nerv. & Ment. Dis., Proc. **8**:182, 1927.

9. Kahn, A. J.: Effects of Variations in Intracranial Pressure, Arch. Neurol. & Psychiat. **51**:508 (June) 1944.

treme degree of edema of the brain was produced by the perfusion of distilled water in the common carotid artery of animals. During the experiments the cisternal and the intraventricular pressure were simultaneously recorded.

A high intraventricular and a relatively low cisternal pressure were constantly observed. This disparity was interpreted as probably due to herniation of the brain stem into the foramen magnum or through the incisura tentorii, with the creation of a resulting partial block between the lateral ventricles and the cisterna magna. The circulatory and respiratory embarrassment associated with high levels of intraventricular pressure could be relieved by ventricular drainage. No circulatory or respiratory embarrassment occurred when both the cisternal and the intraventricular pressure were at high levels; medullary embarrassment appeared soon after the cisternal pressure was lowered, the intraventricular pressure alone remaining high.

CLINICAL CONCLUSIONS

What additional therapeutic conclusions are to be derived from the pathologic observations described in this study? The following significant clinical points should be stressed:

The herniation of the hippocampal gyrus, so often observed in cases of increased intracranial pressure, cannot in itself be considered responsible for the gravity and danger of the clinical syndrome. Histopathologic analysis of the reported cases revealed that most of the clinical symptoms and the frequently observed sudden death after lumbar puncture must be ascribed to the frank herniation of the rostral portion of the brain stem into the tentorial opening, followed by far advanced destruction of the brain stem.

Transtentorial herniation of the brain stem presents a grave danger and hazard for the clinician and the neurosurgeon. It is evident that lumbar puncture and pneumoencephalography must be interdicted if the existence of the herniation of the brain stem has been clinically recognized or suspected.

Transtentorial herniation of the brain stem explains in some instances the fact that lumbar pressures are not always a true index of intraventricular pressure.

Patients with lesions of the temporal lobe appear to be graver clinical risks, probably because of the possible tendency toward development of transtentorial herniation of the brain stem. Therefore, such manipulative procedures as lumbar puncture or pneumoencephalography are attended with greater risks.

It has been assumed in cases of supratentorial tumor in which death followed lumbar puncture that cerebellar herniation into the foramen magnum was responsible. However, it has not been explained how the intraventricular pressure could be transmitted to the posterior fossa. The present study indicates that transtentorial hernia of the brain stem is the important factor. The absence of formation of cerebellar pressure cone in the present group of cases corroborates my conclusions.

Clinical and pathophysiologic evidence has been accumulated to prove that the hypothalamic nuclei contain the higher regulatory centers for respiratory and cardiac control. It appears that transtentorial herniation of the brain stem might result in an interruption of the cardiorespiratory pathways between the diencephalic and the medullary centers and might be responsible for the so-called neurovegetative disturbances, namely, irregularities in respiration and pulse, hyperthermia and sudden cessation of respiration, with a rapid, bounding, and often irregular, pulse.

Attempts to release the temporal pressure cone by removal of the herniated portion of the gyrus hippocampus has been suggested by Jefferson.[2] The observations presented in this study suggest that section of the free edge of the rigid tentorium should be undertaken in an effort to distribute pressure more evenly. In many cases, particularly of tumor of the temporal lobe, this is technically possible.

It is conceivable that in certain cases the establishment of ventricular drainage might prove to be a life-saving measure, pending a more definitive operative attack.

SUMMARY

In 55 cases of transtentorial herniation of the brain stem complicating arterial hypertension, cerebral arteriosclerosis, cerebral trauma, brain tumor or brain abscess, the herniation was associated with hemorrhages and edema of the brain stem.

Hemorrhages of the brain stem are predominantly perivenous and are believed to be due to an extreme state of venous congestion, caused by compression and strangulation of the venous system draining the midbrain.

In view of the gravity of the clinical symptoms resulting from the transtentorial herniation of the brain stem, the establishment of ventricular drainage or section of the free edge of the rigid tentorium, in an effort to distribute pressure more evenly, may be a life-saving measure, pending final, and more radical, treatment.

Cincinnati General Hospital.

LIPOMA OF THE BRAIN

REPORT OF CASES

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Lipomas of the brain, because of their extreme rarity and the fact that most of them do not cause symptoms or signs during life, are clinically unimportant tumors. Most of them are unexpectedly encountered at necropsy. Up to this time the literature, as far as we could ascertain, does not contain data on any case of lipoma of the brain which was subjected to surgical attack. The chief interest in this lesion lies in its origin, and there have been a host of speculations in this regard.[1]

Lipoma of the brain has been discovered in 2 cases at the Mayo Clinic. In 1 of these cases the lesion was productive of symptoms which led to surgical removal.

REPORT OF CASES

CASE 1.—A woman student aged 18 registered at the Mayo Clinic on Jan. 17, 1933, because of attacks of unconsciousness, loss of memory and powers of concentration, and obesity.

The family history was noncontributory, and the patient had been entirely well until February 1928, when she was discovered unconscious in bed one morning. She aroused from this attack and was able to attend school that day. In June 1928 and June 1929 she had similar attacks. One day in December 1929 she ran to her father, saying she felt dizzy and faint. She promptly fell into coma but again quickly recovered. Some time during 1929 she first menstruated, and it was observed that she was gaining more weight than was considered desirable. Her memory and powers of concentration began to fail at about this time, and she had difficulty in school. In November 1932 a generalized convulsion was followed by severe headache. Early in January 1933 another attack of unconsciousness occurred. During the two years prior to her registration at the clinic she experienced intermittent frontal headaches, which disappeared after she took acetylsalicylic acid.

The patient was 63 inches (160 cm.) tall and weighed 152 pounds (68.9 Kg.). The systolic blood pressure varied between 96 and 88 mm. of mercury. The pulse rate was 60 beats per minute. There were no other general physical findings of importance. Neurologic examination revealed only a mild tremor of both hands. Examination of the eyes, including the visual fields, gave normal results. The results of routine tests on the blood and urine were within normal limits. The roentgenogram of the head (fig. 1) showed a large mass, measuring approximately 5 by 8 cm., in the midline in the frontal fossa. Calcification in its walls outlined it rather well. A diagnosis of congenital cyst with calcified walls was made.

On Jan. 23, 1933 the patient was anesthetized with ether and a long coronal incision was made back of the hair line. The scalp and periosteum were reflected from the bone in one layer, and a block of bone, measuring 12 cm. from front to back and extending 6 cm. on each side of the midline, was removed from over the frontal lobes. After the dural opening was made and the falx cerebri exposed, the right frontal lobe was retracted laterally; in the depths of the wound lay an encapsulated, fibrous, fatty mass, which extended from beneath the anterior extremity of what remained of the corpus callosum. The anterolateral limits of the tumor were reached on each side by clipping and coagulating branches of the anterior cerebral arteries and pushing the brain away from the surface of the mass. Then the anterior portion of the falx was divided, after ligation of the superior and inferior longitudinal sinuses, and the tumor was almost entirely removed together with a part of the corpus callosum. To accomplish this it was necessary to divide the left anterior cerebral artery. Several veins draining the left frontal lobe at its anterior pole were also interrupted. A mass similar to the main one, although much smaller, was removed from the choroid plexus of the left lateral ventricle. The surgical specimens are shown in figure 2.

The tumor was composed of adult adipose tissue which in some parts bore more stroma than ordinary

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From the Section on Neurosurgery, Mayo Clinic.

1. (*a*) Bostroem, E., cited by Sperling and Alpers.[1g] (*b*) Ehni, G., and Love, J. G.: Intraspinal Lipomas: Report of Cases, Review of the Literature and Clinical and Pathologic Study, Arch. Neurol. & Psychiat. **53**: 1-28 (Jan.) 1945. (*c*) Gowers, W. R.: Myo-Lipoma of the Spinal Cord, Tr. Path. Soc. London **27**:19-22, 1876. (*d*) Krainer, L.: Die Hirn- und Rückenmarkslipome, Virchows Arch. f. path. Anat. **295**:107-142 (Feb.) 1935. (*e*) della Rovere, D., cited by Ritter.[11] (*f*) Scherer, E.: Ueber die pialen Lipome des Gehirns; Beitrag eines Falles von ausgedehnter meningealer Lipomatose einer Grosshirnhemisphäre bei Mikrogyrie, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:45-61 (July) 1935. (*g*) Sperling, S. J., and Alpers, B. J.: Lipoma and Osteolipoma of the Brain, J. Nerv. & Ment. Dis. **83**: 13-21 (Jan.) 1936. (*h*) Stookey, B.: Intradural Spinal Lipoma: Report of a Case and Symptoms for Ten Years in a Child Aged Eleven; Review of the Literature, Arch. Neurol. & Psychiat. **18**:16-42 (July) 1927.

adipose tissue. The fat was rather vascular, containing many small arteries and veins, but was not angiomatous. A fibrous septum separated the fat from the neural substance and sent projections into the brain substance. The small mass from the left choroid plexus was composed of adult adipose tissue which was more fibrous and cellular than ordinary fat and which lay within the plexus without any evident encapsulation by connective tissue. In certain portions of the larger tumor great quantities of small and medium-sized calcified spherules, which resembled psammoma bodies, lay in the connective tissue, and even in the brain substance bordering on the tumor (fig. 3 *a* and *b*).

After the operation the patient remained comatose; the legs were in strong extension; the arms were

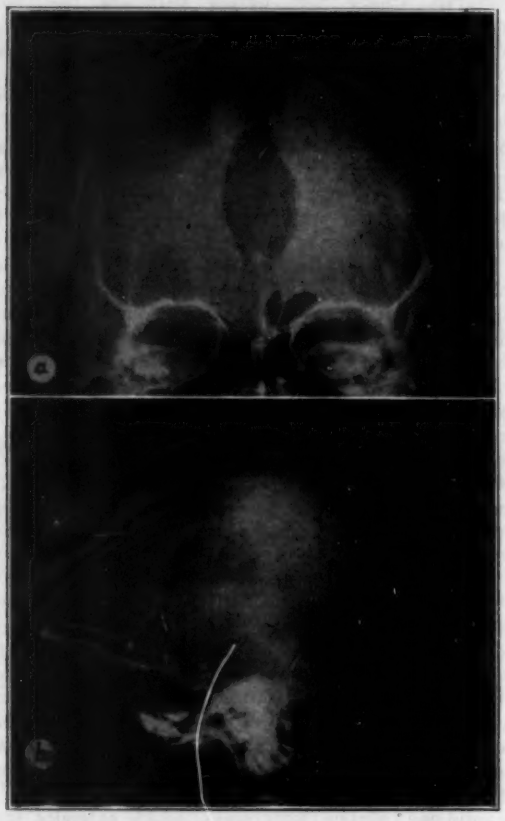

Fig. 1 (case 1).—(*a*) Posteroanterior view of the head, showing a crescentic band of calcification on each side of the midline, with the concave borders facing each other. One side is almost a mirror image of the other. (*b*) Lateral view of the head, showing a broad, angular band of calcification lying in the general position of the rostrum of the corpus callosum.

flexed on the chest, and static tremors occurred in all parts of the body except the head and neck. The course was progressively downhill, and she died the fifth day after operation.

Necropsy revealed infarction of the left frontal lobe, with thrombosis of the veins over the surface. The superior longitudinal sinus was patent posterior to the point of ligature. A cavity, measuring 4 by 4 by 5 cm., lay beneath the site from which the rostrum of the corpus callosum was removed. This cavity communicated with the lateral and third ventricle. Remnants of the tumor remained in the walls. Otherwise nothing of significance was noted.

Case 2.—A girl aged 16 years registered at the Mayo Clinic on March 10, 1937, complaining of headaches, vomiting, vertigo and drowsiness.

The family history was noncontributory, and the patient had been perfectly well until December 1936, when she began to have occasional headaches in the morning; these lasted from a few hours to all day. They were usually frontal and had not been severe until the month prior to her registration. On March 3, 1937 she discontinued attendance at school because of the headaches. The next day vertigo developed. On March 5 she vomited and thereafter continued to do so three or four times a day. On March 6 the headache became worse and extended to the suboccipital and cervical region. The pain was even felt down to the left arm. On March 7 she noticed tinnitus and staggering to the left in walking. On March 8 she was hospitalized in her home town but two days later was brought to the clinic, when paralysis of the extraocular muscles and drowsiness set in.

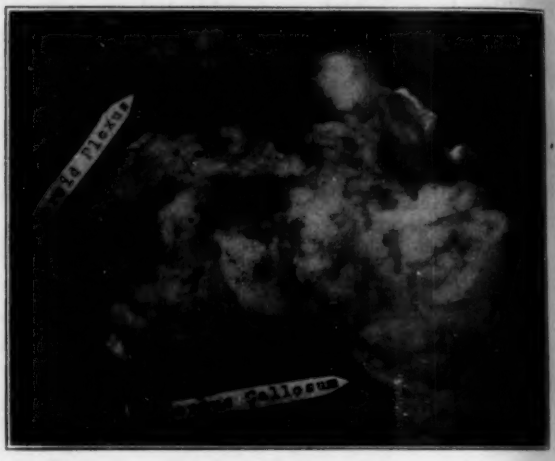

Fig. 2 (case 1).—Tissue removed at operation.

On her admission to the clinic the patient was drowsy but cooperative and was obviously extremely ill. The significant findings were mild horizontal nystagmus, bilateral papilledema of 3 D., bilateral paralysis of the oculomotor and facial nerves, dysarthria, incoordination of the left arm, stiff neck and a moderately strong Kernig sign on both sides. Sensation was normal; there were no signs referable to the pyramidal tract, and the visual fields were grossly normal. The urine contained a moderate amount of albumin, a moderate number of pus cells and some erythrocytes. The concentration of urea was 20 mg. per hundred cubic centimeters of blood. The leukocytes numbered 16,600 per cubic millimeter of blood, and the hemoglobin measured 14 Gm. per hundred cubic centimeters of blood. Roentgenograms of the head and chest revealed nothing abnormal.

On the day after her registration the systolic blood pressure gradually rose and the patient became less and less responsive. The next day she was comatose; the temperature rose to 102 F., and she died.

Necropsy disclosed an extensive carcinomatous change throughout the mucosa of the stomach. This organ was studded with small nodules, measuring from 2 to

5 mm. in diameter, composed of malignant, mucus-containing, signet ring cells. Metastatic lesions were observed in the liver, spleen, colon, periadrenal fat, renal pelves, bladder, vagina, cervix, ovaries, mesenteric nodes, thymus, epicardium, lungs, hilar nodes of the lungs, thyroid, axillary nodes and cerebral meninges and in a small lipoma lying on the corpus callosum. This lipoma, which was 3 cm. long and from 5 to 8 mm. in diameter, lay on the posterior half of the corpus callosum. It had no firm attachments to the gyri cinguli or the corpus callosum (fig 4 *a* and *b*) and was too small to be of any consequence.

COMMENT

Of most importance in case 1 was the fact that the lesion was mistaken for a cystic tumor with calcified walls. Because of this error the roentgenograms were examined again. They showed a thick calcified layer in both the postero-anterior and the lateral exposure. The lateral view seemed to provide a profile of the rostrum of the corpus callosum. The thick calcified layer differed considerably from the fine line of calcium observable in the roentgenogram in cases of craniopharyngioma and may be a basis for future differentiation.

With a tumor of such size and in such a complex location it is impossible to say from what the lesion arose—whether from the corpus callosum, the lamina terminalis, the choroid plexus or some other structure. To be safe, we have classified the tumor as originating in the choroid plexus or the ventricular wall, although it may have come from the rostrum of the corpus callosum.

In case 2 the features which concerned the lipoma were not extraordinary. It is inconceivable that the lipoma and the carcinoma of the stomach were related, though this combination has been remarked on by others.[1e]

The subject of lipoma of the brain has been reviewed a number of times, but most recently by Krainer.[1d] This author was able to study reports of 56 cases of such tumors. The cases in his tables total 57, but he duplicated the case of Chouppe[2] by listing it as no. 25 and again as no. 50. To these 56 cases should be added a number of other cases in order to bring the total up to date. The cases of Weber and Daser,[3] Scherer,[1f] Baker and Adams,[4] Sperling and

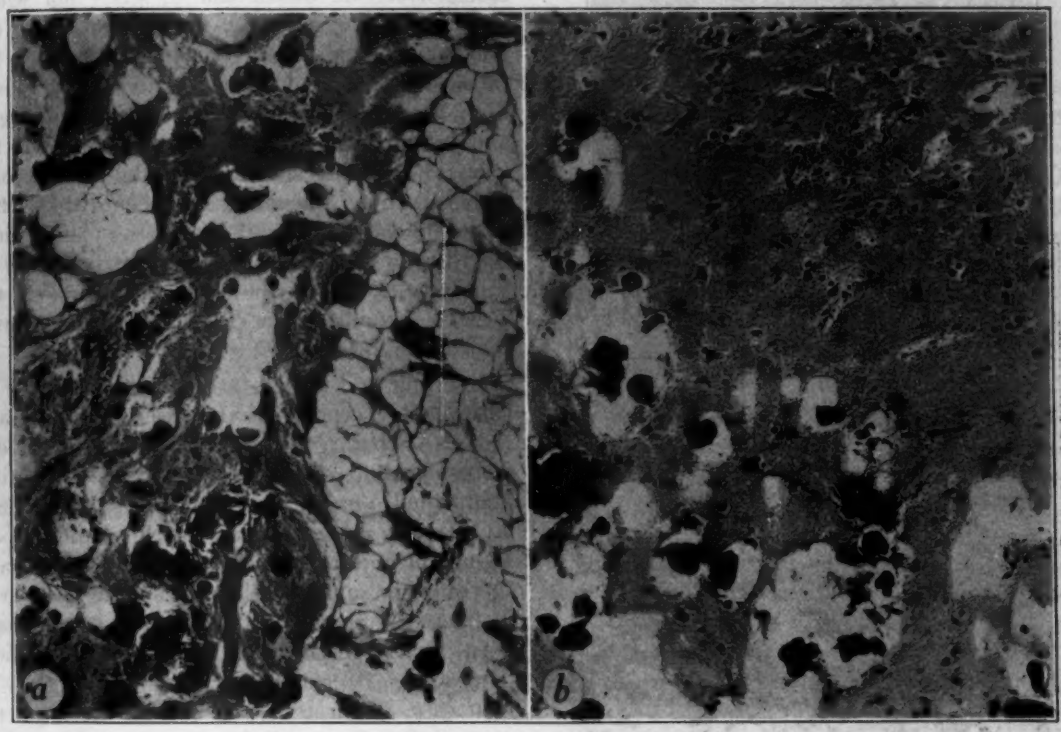

Fig. 3 (case 1).—(*a*) Portion of the fibrous capsule of the larger tumor. The adult adipose tissue is bordered by a heavy capsule of collagen, which contains islands of fat cells and numerous lamellated calcified bodies. (*b*) Portion of the brain bordering the tumor. Numerous calcified bodies are lying in the neural substance, without any surrounding fibrous tissue. Hematoxylin and eosin stain; × 85.

2. Cited by von Sury.[6]

3. Weber, F. P., and Daser, P.: Osteo-Lipoma of the Brain Arising from the Infundibulum, Tr. Path. Soc. London **58**:219-225, 1907.

4. Baker, A. B., and Adams, J. M.: Lipomatosis of the Central Nervous System, Am. J. Cancer **34**: 214-219 (Oct.) 1938.

Alpers [1g] and Rubinstein [5] are genuine instances of this lesion and may be added without argument. According to von Sury,[6] Rokitansky [2] described a case in addition to the one accepted by Krainer, and there seems no good reason for not including this case in the total. Misch [7] reported 2 cases of intracranial lipoma, but only in the second was the tumor intradural, probably originating in the pia. This case should be added to the total. Scherer [1f] referred to cases described by Simon,[8] but all that can be learned is that Simon reported 2 cases of lipoma of the clivus and 1 case of lipoma of the plexus. Whether the 2 lipomas of the clivus were extradural, as was the tumor in the first case reported by Misch, can only be surmised, but the remaining case is probably pertinent to the present discussion. Krainer merely listed 5 additional cases, which he was unable to study but which were evidently accepted by others.[9] He did not include the case reported by Shaw [10] because he considered the lesion to be extradural. Shaw stated that the tumor was in the meninges, and in his anatomic description he related the mass to the bony structures of the middle fossa rather than to the brain. It seems that when the brain was removed the tumor was left behind. Sperling and Alpers [1g] accepted Shaw's case as genuine. Without the case of Shaw or the 2 cases of tumor of the clivus reported by Simon the total number is 69.

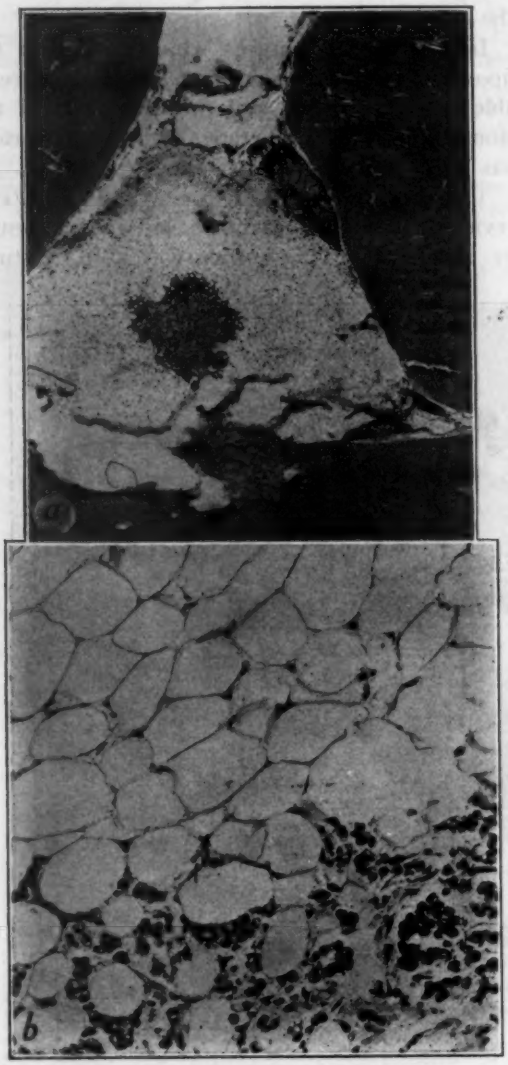

Fig. 4 (case 2).—Tissue from the lipoma: (*a*) Section through the entire lipoma (× 9). The corpus callosum lies below, and to either side are the gyri cinguli. In the center of the lipoma and at the upper right aspect are carcinomatous nodules metastatic from the stomach. The origin appears to be from the dorsal surface of the corpus callosum, but smaller islands of carcinomatous cells and an artefactitious separation obscure the point of origin. (*b*) Portion from the center of the lipoma, showing the adult adipose tissue above and the edge of the carcinomatous nodule below (× 135). The eccentric position of the nuclei in the mucus-containing, signet ring cells in the metastatic lesion from the stomach may be noted. Hematoxylin and eosin stain.

Sperling and Alpers arrived at a total of 74 cases before reports of the cases of Baker and Adams,[4] Scherer,[1f] Krainer,[1d] Misch [7] and Simon [8] were available. To arrive at their figure, they augmented Verga's list.[1a] Certain of the cases added to Verga's list by Sperling and Alpers should be omitted. The cases of Ritter [11] and Oppenheim and Borchardt [12] were primarily instances of lipoma of the spinal cord and have been properly classified in reports on this lesion. The case of "Verfasser" is in reality von Sury's [6] own case, duplicated by a curious error on the part of Sperling and Alpers. Von Sury used the word *Verfasser* ("author") in his tabulations to refer to the case he had just reported, and Sperling and Alpers evidently accepted the

5. Rubinstein, B. G.: Ueber einen Fall von unvollständig fehlendem und durch Fettgewebe ersetztem Balken, Frankfurt. Ztschr. f. Path. **44**:379-386, 1932.

6. von Sury, K.: Ein gemischtes Lipom auf der Oberfläche des hypoplastischen Balkens, Frankfurt. Ztschr. f. Path. **1**:484-491, 1907.

7. Misch, W.: Meningeal Lipomas in the Foramen Magnum, J. Neurol. & Psychopath. **16**:123-129 (Oct.) 1935.

8. Simon, cited by Scherer.[1f]

9. Footnotes 1 *a* and 6.

10. Shaw, R. H.: Ptosis Produced by Intracranial Lipoma, Brit. M. J. **2**:1828 (Dec. 26) 1896.

11. Ritter, A.: Ein Lipom der Meningen des Cervicalmarks, Deutsche Ztschr. f. Chir. **152**:189-209, 1920.

12. Oppenheim, H., and Borchardt, M.: Weiterer Beitrag zur Erkennung und Behandlung der Rückenmarksgeschwülste, Deutsche Ztschr. f. Nervenh. **60**: 1-32, 1918.

word as the name of an additional author. In Virchow's [13] case a dural tumor of some sort was present, but it was not a pial or a ventricular tumor, and therefore we did not include it in our total.

Haverfield and Walker [14] have reported a type of tumor which we rigidly exclude from classification with pial lipomas. Although these authors stated that their tumor and other lipomatous meningiomas do not differ from the lipoma outside the central nervous system, our opinion is to the contrary, and the histologic study of their own tumor contradicts them. They reported that portions of their tumor were composed of meningotheliomatous cells—certainly not to be found in the ordinary lipoma. We have had experience with meningiomas of this sort and though many of the cells may be fatty, even to the point of resembling the cells of adult adipose tissue, the true nature of the tumor is indicated by the presence of sheets of nonadipose cells and whorl-like formations. The most striking gross distinction between fatty meningioma and true lipoma is the lack of dural attachment in the lipoma. True lipoma of the nervous system is similar to lipomas outside the nervous system except that it frequently displays calcification, or even bone.

The 69 cases we found in our partial review of the literature and the 2 cases reported in this communication bring the total to 71 reported cases. Krainer chose to relate the tumors he studied to the various intracranial cerebrospinal fluid cisterns. Though this method of investigation was pertinent to the development of his thesis, the problem seems clearer to us if 70 of the tumors are tabulated according to the structure from which they arose, with the following result: Twenty-five arose from the corpus callosum; 18, from the ventral diencephalic structures; 9, from the choroid plexus or the walls of the lateral and third ventricles; 7, from the dorsal portion of the midbrain; 1, from the ventral portion of the midbrain; 4, from the medulla; 4, from the pons and structures of the cerebellopontile angle, and 2, from the cerebral convexities. Six of the tumors which arose from the corpus callosum were accompanied by one or more additional tumors of the choroid plexus, and 1 was accompanied by a tumor of the olfactory nerve.

13. Virchow, R.: Ein Fall von bösartigen, zum Theil in der Form des Neuroms auftretenden Fettgeschwülsten, Virchows Arch. f. path. Anat. **11**:281-288 (March) 1857.

14. Haverfield, W. T., and Walker, A. E.: Lipoblastic Meningioma, Arch. Surg. **42**:371-378 (Feb.) 1941.

One of us, with Love,[1b] has discussed in some detail the problem of the origin of lipoma of the pia mater in connection with intraspinal lipoma; since the problem which concerns lipoma of the brain is the same, it will be adequate merely to list the various mechanisms suggested to account for such a fatty mass. They are: (1) proliferation of the few fat cells normally present in the leptomeninges; (2) deposition of fat in cellular masses arising from proliferation of common connective tissue cells; (3) deposition in connective tissue or glia of fatty products of the breakdown of nerve tissue; (4) fatty degeneration of proliferated glia; (5) abnormal inclusion of fat-forming material within the closing lips of the neural groove, and (6) perverted differentiation of persisting embryonic meninx.

Scherer amplified the last-mentioned mechanism by indicating the probable primitive cells responsible for the formation of the fat—an adaptation of Wassermann's [15] researches. One of us, with Love,[1b] has further amplified this mechanism by suggesting that the primitive cells with fat-forming potentialities are permitted to form fatty masses by a defect in the neural crest. This fundamental defect results in failure of local control of formation of fat, and the stage is set for the lipoma to develop.

The gross and microscopic features of pial lipoma are not significantly different from those of lipoma in other locations except that intracranial lipoma may contain calcified material ranging from psammoma bodies to true bone. In case 1 of this report calcification was present even in the brain substance adjacent to the tumor. The significance of this observation is unknown. An intraspinal pial lipoma containing calcium has not been discovered.[1b]

The clinical importance of the intracranial pial lipoma remains slight even with the demonstration that a tumor of this type may produce symptoms, give roentgenographic evidence of a confusing nature and be subjected to removal. The lesion is merely to be remembered in the differentiation of calcified tumors of the brain.

SUMMARY AND CONCLUSIONS

In 1 of 2 cases of lipoma of the brain described in this paper the tumor caused symptoms of brain tumor, contained enough calcium to cast a shadow in the roentgenogram and was removed surgically.

15. Wassermann, F.: Die Fettorgane des Menschen. Entwicklung, Bau und systematische Stellung des sogenannten Fettgewebes, Ztschr. f. Zellforsch. u. mikr. Anat. **3**:235-328, 1926.

With the 2 cases reported in this paper, 71 cases of lipoma of the brain or intradural cranial nerves have been reported in the literature. The favored sites of origin, in their order of frequency, are the corpus callosum, the ventral diencephalic structures, the choroid plexus or ventricular walls of the lateral and third ventricles and the dorsal surface of the midbrain.

The mechanism of formation of this lipoma is probably a perversion of differentiation of the primitive meninges. Elements with fat-forming potentialities are present in the meninges, and the lipoma develops when the ectodermal mesenchyme contributing to the leptomeninges is defective.

This tumor has slight clinical importance, but it must be added to the list of lesions requiring differentiation when calcium is discovered on roentgenologic examination.

The Mayo Clinic.

BROMINE CONTENT OF THE BLOOD IN MENTAL DISEASES

I. DEMENTIA PRECOX

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Bromide therapy has been used for many years in the treatment of conditions associated with psychomotor disturbance and increased vasomotor irritability. From time to time the bromide content of the blood of patients with such disorders has aroused the interest of investigators. In 1931 Zondek and Bier [1] reported that in 29 of 34 patients with manic-depressive psychoses who were examined the bromine content of the blood was from 40 to 60 per cent below the normal value (1 mg. per hundred cubic centimeters) previously established by them. The average value for the 34 patients was 0.572 mg. per hundred cubic centimeters. They also stated that in 5 out of 17 patients with schizophrenia studied the blood bromides were low. In 1933 the same authors [2] concluded that the bromide content of the blood of patients with mental disease was likely to be low and discussed the concentration for 6 mentally depressed patients.

Klimke and Holthaus [3] presented the cases of 6 patients with psychomotor disturbances and concluded that lowering of the blood bromides was characteristic and proportional to the intensity of the disturbance. Sacristan and Peraiata [4] analyzed the blood of 13 women with manic-depressive psychoses and in every case found the bromine content to be less than the accepted normal. Ten women with other psychoses were also studied, but no deviation from normal values for blood bromide was noted. On the basis of these results, these investigators concluded that the bromide concentration of the blood was lowered in patients with manic-depressive insanity. Since all these investigators had used methods which were later shown to be unreliable, the validity of their conclusions is open to question.

In 1933 Hennelly and Yates,[5] using a new and more accurate method of analysis of their own, obtained low values for the bromine of the blood for males with schizophrenia of all types, paraphrenia, manic-depressive psychoses and involutional melancholia, while the values for patients with psychoneuroses and organic dementia were within the normal range. These investigators placed little reliance on the estimation of the bromine content of the blood in the diagnosis of manic-depressive psychosis, since no correlation between the stage of the mental disease and variation in the bromine content of the blood could be obtained. These observations were based on the study of 56 patients, including 11 mentally normal patients, as well as the patients with mental disease noted.

Meier and Schlientz [6] used the method of Leipert for the analysis of blood bromides for 35 patients with psychoses. For 27 patients with nonbromide medication the bromine content ranged from 75 to 233 micrograms per hundred cubic centimeters, with an average value of 132 micrograms. Pierre and Camille Chatagnon,[7] also reporting in 1936, stated that for 23 of 31 patients with manic-depressive psychosis which they had studied the bromine values were higher than normal.

Because of the unreliability of the methods used by some of the previous investigators, and because of the few cases of any one type of mental condition included in the reports of any of these workers, we decided to make an extensive study of the bromine content of the blood of various types of mentally disturbed patients. The first investigation was restricted to patients with dementia precox. The subjects chosen had all

From the Department of Physiological Chemistry, Ohio State University College of Medicine.

The present investigation was made possible through the staff of the Columbus State Hospital for the Insane, Dr. J. F. Bateman, Superintendent.

1. Zondek, H., and Bier, A.: Brom im Blute bei manisch-depressivem Irresein, Biochem. Ztschr. **241**: 491, 1931.

2. Zondek, H., and Bier, A.: Brom in Blute bei Psychosen, Klin. Wchnschr. **12**:55, 1933.

3. Klimke, W., and Holthaus, B.: Ueber den Bromspiegel des Blutes bei psychomotorischen Erregungszuständen, Deutsche med. Wchnschr. **58**:1558, 1932.

4. Sacristan, J. M., and Peraiata, M.: Ueber den Bromspiegel des Blutes bei manisch-depressivem Irresein, Klin. Wchnschr. **12**:467, 1933.

5. Hennelly, T. J., and Yates, E. D.: Blood Bromine in the Psychoses, J. Ment. Sc. **81**:173, 1935.

6. Meier, C. A., and Schlientz, W.: Neure Untersuchungen über den Bromspiegel im Blut bei Psychosen, Klin. Wchnschr. **15**:1845, 1936.

7. Chatagnon, P., and Chatagnon, C.: Le métabolism du brome dans l'organism humain, Compt. rend. Acad. d. sc. **202**:1119, 1936.

been inmates of the Columbus State Hospital for the Insane for more than three months, while some had been in residence there for more than ten years.

A method of bromine analysis previously devised by one of us (H. L. W.)[8] was used in this investigation. The accompanying table gives the results for 172 patients with dementia precox.

Although the values in the table range from 0.09 to 1.60 mg. of bromine per hundred cubic centimeters of whole blood, nevertheless the values in few cases approached these limits. The figures for 80 per cent of the subjects differing from this value by less than 0.2 mg. per hundred cubic centimeters. The bromine content of the blood of patients with dementia precox included in the present study therefore appears to be consistently lower than that of normal healthy persons residing in the same geographic area. Differences in blood bromine content of the two groups cannot be attributed entirely to differences in bromide intake in food or water, since the same sources were available to the two groups.

Bromine Content of the Blood of One Hundred and Seventy-Two Patients with Dementia Precox

Case No.	Age, Yr.	Bromine per 100 Cc. Whole Blood	Case No.	Age, Yr.	Bromine per 100 Cc. Whole Blood	Case No.	Age, Yr.	Bromine per 100 Cc. Whole Blood	Case No.	Age, Yr.	Bromine per 100 Cc. Whole Blood
Males			Males			Males			Males		
1	62	0.55	45	37	0.56	89	24	0.49	133	22	0.56
2	60	0.45	46	25	0.36	90	59	0.52	134	59	0.69
3	63	0.58	47	57	0.77	91	40	0.47	135	39	0.40
4	65	0.41	48	35	0.50	92	45	0.62	136	39	0.69
5	75	0.77	49	32	0.38	93	59	0.54	137	24	0.68
6	54	1.00	50	30	0.79	94	55	0.51	138	34	0.68
7	61	0.72	51	34	0.54	95	28	0.56	139	66	0.76
8	77	0.69	52	33	0.42	96	50	0.59	140	50	0.75
9	40	0.56	53	33	0.46	97	27	0.65	141	56	0.48
10	59	0.73	54	35	0.09	98	34	0.52	142	31	0.64
11	48	0.71	55	32	0.56	99	37	0.47	143	35	0.69
12	62	0.59	56	32	0.59	100	37	0.50	144	22	0.47
13	58	0.79	57	32	0.54	101	31	0.60	145	29	0.58
14	55	0.69	58	34	0.38	102	40	0.36	146	64	0.57
15	49	0.43	59	36	0.32	103	33	0.79			
16	45	0.53	60	40	0.56	104	29	0.23			
17	56	0.75	61	62	0.29	105	37	0.67	Females		
18	59	0.69	62	27	0.60	106	52	0.57			
19	46	0.67	63	36	0.55	107	23	0.72	1	62	1.00
20	53	0.36	64	27	1.00	108	44	0.37	2	40	0.50
21	57	0.49	65	47	0.70	109	27	0.45	3	50	0.69
22	47	0.73	66	75	0.70	110	59	0.14	4	32	0.33
23	45	0.59	67	47	0.73	111	29	0.65	5	42	0.56
24	70	0.50	68	30	0.66	112	20	0.54	6	26	0.33
25	50	0.48	69	19	0.39	113	17	0.45	7	35	0.42
26	56	0.63	70	37	0.60	114	31	0.43	8	36	0.35
27	47	0.52	71	46	0.71	115	42	0.79	9	33	0.45
28	49	0.76	72	46	0.79	116	21	1.60	10	34	0.36
29	57	0.18	73	32	0.44	117	37	0.68	11	38	0.93
30	42	0.42	74	30	0.69	118	27	0.58	12	43	0.41
31	62	0.45	75	66	0.45	119	39	0.59	13	25	0.37
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33	40	0.46	77	32	0.59	121	25	0.38	15	58	0.42
34	34	0.42	78	26	0.68	122	28	0.59	16	27	0.41
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37	37	0.56	81	34	0.79	125	31	0.64	19	29	0.40
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39	36	0.56	83	31	0.85	127	33	0.34	21	35	0.49
40	68	0.16	84	66	0.69	128	23	0.37	22	51	0.35
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44	34	0.67	88	38	0.75	132	59	0.69	26	41	0.35

values for 64 patients (37.2 per cent) differed from the average value (0.555 mg. of bromine per hundred cubic centimeters) by less than 0.1 mg., while the values for 138 patients (80.2 per cent) were within 0.2 mg. of the average.

A previous study[9] of the bromine content of the blood of normal healthy persons residing in Columbus revealed an average value of 0.81 mg. of bromine per hundred cubic centimeters, with

8. Wikoff, H. L.; Bame, E., and Brandt, M.: A Method for the Determination of Bromine in a Protein-Free Filtrate, J. Lab. & Clin. Med. **24**:427, 1939.

9. Wikoff, H. L.; Brunner, R. A., and Allison, H. W.: The Normal Bromine Content of the Blood of Healthy Individuals, Am. J. Clin. Path. **10**:234, 1940.

SUMMARY

The average bromine content of the blood of 172 patients with dementia precox was found to be 0.555 mg. of bromine per hundred cubic centimeters of blood. It is significant that the values for 80.2 per cent of the patients examined varied from the average (0.555 mg.) by less than 0.2 mg. The average value for the patients with dementia precox was lower than the average obtained by the same method for normal persons residing in the same city.

Drs. Rothermich, Michael and Whittenbrook selected the patients and furnished the diagnoses for this study.

Ohio State University College of Medicine.

SKULL DEFECT AND HERNIATION OF CEREBRUM WITH ABSENCE OF DURA FOLLOWING HEAD INJURY IN ADOLESCENCE

CAPTAIN WILLIAM S. McCUNE
AND
MAJOR BARNES WOODHALL
MEDICAL CORPS, ARMY OF THE UNITED STATES

A few cases of delayed absorption in bones of the skull following head injury have been described. Pancoast, Pendergrass and Schaeffer [1] reported a case in which an unusual alteration in bony structure developed after a fracture of the skull, with hernia of the cerebrum and elevation of a fragment of bone from the cranium. Rowbotham [2] described a defect in the vault of the skull with traumatic malacia or absorption of bone following a closed head injury. The thinning and scalloping of bone adjacent to a comminuted fracture of the skull, characteristic of traumatic cyst of the leptomeninges, is not unusual. It was well portrayed by Dyke [3] and has been duplicated in our series of head injuries. However, in a review of the literature we have been able to find no instance of a defect in the inner table of the skull alone with herniation of the brain and absence of dura mater following head injury. Having encountered such a case, we present it as an aid in the differentiation of lesions of this type from tumors and infections of the skull.

REPORT OF A CASE

History—A private in the Women's Army Corps, aged 32, was admitted to the Walter Reed General Hospital on Feb. 10, 1944, as a transfer from the station hospital at Fort George G. Meade, Md., because of headache, fainting spells and the presence of an irregular area of destruction of bone in the left parietal area of the skull.

She stated that at the age of 15 (in 1927), while walking along a country road one evening, she had been knocked down by a passing automobile, which struck the left side of her head. She was unconscious for twenty or thirty minutes. She received medical care and was kept in bed for two weeks, but no roentgenograms of the skull were taken. Except for mild, transient frontal headaches, she was well after the accident until 1939. During that year headaches, which were not lateralized and not accompanied by vomiting, became more severe and recurred two or three times a month, each attack lasting about twelve hours. Under a regimen of rest the attacks subsided again, only to recur in 1943, after she had enlisted in the Women's Army Corps. In November 1943, one month after enlistment, she felt dizzy one day while marching to a class and fainted on reaching the school where the classes were held. She did not have a convulsion and was unconscious for only five minutes. Later in the same month, while drilling one day, she fainted again, and she had two similar episodes on Jan. 17 and Jan. 18, 1944, without convulsive movements, biting of the tongue or incontinence. Examination at the Fort George G. Meade Station Hospital revealed only an equivocal Babinski sign on the right side. Because of the finding of an irregular defect in the left parietal bone, however, she was transferred to the Walter Reed General Hospital for further study, arriving there on February 10.

Examination.—Physical examination on admission to the hospital revealed no evidence of acute disease. There was slight tenderness over the left parietal area of the skull on tapping or pressure. The blood pressure was 110 systolic and 76 diastolic. General physical examination revealed nothing abnormal except for a small mass in each pelvic vault. Neurologic examination showed no significant abnormalities.

Roentgenograms of the skull revealed an area of moth-eaten destruction in the left parietal bone, beginning close to the sagittal suture line and extending laterally in the midparietal area for a distance of about 7 cm. (figure, *A*). The anteroposterior diameter was about 4.5 cm., and in the posteroanterior projection the volume of the skull seemed larger on the left side. The inner table alone appeared involved in the diffuse destructive process. There was no increased vascularity in the surrounding bone and no definite involvement of the scalp. The roentgenographic impression was that of cholesteatoma of the left parietal bone. Roentgenograms of the long bones, the pelvis and the thoracic cage showed no abnormalities.

An electroencephalogram recorded a dominant rhythm of 10 per second. There were no seizure discharges and no evidence of a focal lesion. Overventilation pro-

From the Neurosurgical Section, Walter Reed General Hospital, Washington, D. C.

1. Pancoast, H. K.; Pendergrass, E. P., and Schaeffer, J. P.: The Head and Neck in Roentgen Diagnosis, Springfield, Ill., Charles C Thomas, Publisher, 1940.

2. Rowbotham, G. F.: Acute Injuries of the Head, Edinburgh, E. & S. Livingstone, 1942.

3. Dyke, C. G.: The Roentgenological Aspects of Fracture of the Skull and Injuries to the Brain, in Brock, S.: Injuries of Skull, Brain and Spinal Cord, ed. 2, Baltimore, Williams & Wilkins Company, 1943.

Alpers [1g] and Rubinstein [5] are genuine instances of this lesion and may be added without argument. According to von Sury,[6] Rokitansky [2] described a case in addition to the one accepted by Krainer, and there seems no good reason for not including this case in the total. Misch [7] reported 2 cases of intracranial lipoma, but only in the second was the tumor intradural, probably originating in the pia. This case should be added to the total. Scherer [1f] referred to cases described by Simon,[8] but all that can be learned is that Simon reported 2 cases of lipoma of the clivus and 1 case of lipoma of the plexus. Whether the 2 lipomas of the clivus were extradural, as was the tumor in the first case reported by Misch, can only be surmised, but the remaining case is probably pertinent to the present discussion. Krainer merely listed 5 additional cases, which he was unable to study but which were evidently accepted by others.[9] He did not include the case reported by Shaw [10] because he considered the lesion to be extradural. Shaw stated that the tumor was in the meninges, and in his anatomic description he related the mass to the bony structures of the middle fossa rather than to the brain. It seems that when the brain was removed the tumor was left behind. Sperling and Alpers [1g] accepted Shaw's case as genuine. Without the case of Shaw or the 2 cases of tumor of the clivus reported by Simon the total number is 69.

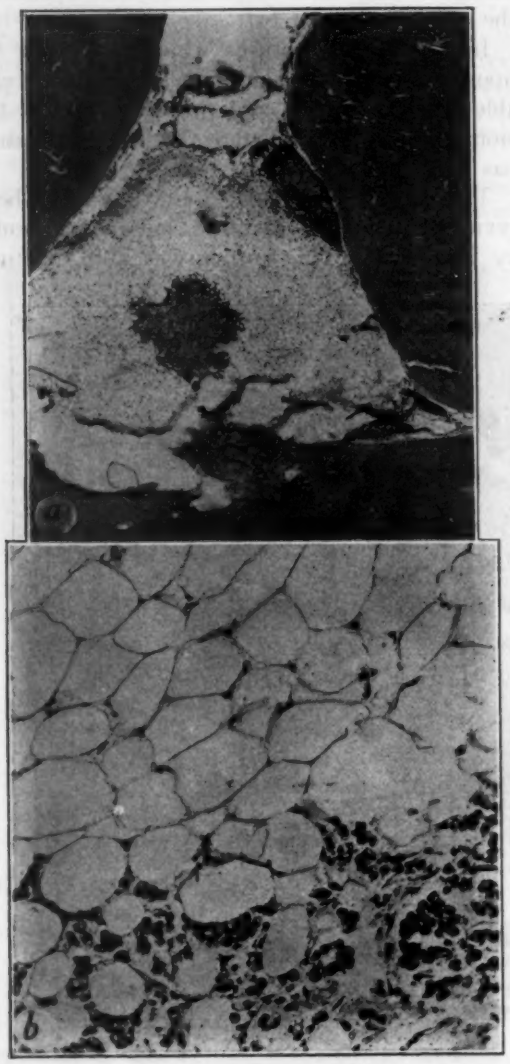

Fig. 4 (case 2).—Tissue from the lipoma: (*a*) Section through the entire lipoma (× 9). The corpus callosum lies below, and to either side are the gyri cinguli. In the center of the lipoma and at the upper right aspect are carcinomatous nodules metastatic from the stomach. The origin appears to be from the dorsal surface of the corpus callosum, but smaller islands of carcinomatous cells and an artefactitious separation obscure the point of origin. (*b*) Portion from the center of the lipoma, showing the adult adipose tissue above and the edge of the carcinomatous nodule below (× 135). The eccentric position of the nuclei in the mucus-containing, signet ring cells in the metastatic lesion from the stomach may be noted. Hematoxylin and eosin stain.

Sperling and Alpers arrived at a total of 74 cases before reports of the cases of Baker and Adams,[4] Scherer,[1f] Krainer,[1d] Misch [7] and Simon [8] were available. To arrive at their figure, they augmented Verga's list.[1a] Certain of the cases added to Verga's list by Sperling and Alpers should be omitted. The cases of Ritter [11] and Oppenheim and Borchardt [12] were primarily instances of lipoma of the spinal cord and have been properly classified in reports on this lesion. The case of "Verfasser" is in reality von Sury's [6] own case, duplicated by a curious error on the part of Sperling and Alpers. Von Sury used the word *Verfasser* ("author") in his tabulations to refer to the case he had just reported, and Sperling and Alpers evidently accepted the

5. Rubinstein, B. G.: Ueber einen Fall von unvollständig fehlendem und durch Fettgewebe ersetztem Balken, Frankfurt. Ztschr. f. Path. **44**:379-386, 1932.

6. von Sury, K.: Ein gemischtes Lipom auf der Oberfläche des hypoplastischen Balkens, Frankfurt. Ztschr. f. Path. **1**:484-491, 1907.

7. Misch, W.: Meningeal Lipomas in the Foramen Magnum, J. Neurol. & Psychopath. **16**:123-129 (Oct.) 1935.

8. Simon, cited by Scherer.[1f]

9. Footnotes 1 *a* and 6.

10. Shaw, R. H.: Ptosis Produced by Intracranial Lipoma, Brit. M. J. **2**:1828 (Dec. 26) 1896.

11. Ritter, A.: Ein Lipom der Meningen des Cervicalmarks, Deutsche Ztschr. f. Chir. **152**:189-209, 1920.

12. Oppenheim, H., and Borchardt, M.: Weiterer Beitrag zur Erkennung und Behandlung der Rückenmarksgeschwülste, Deutsche Ztschr. f. Nervenh. **60**: 1-32, 1918.

word as the name of an additional author. In Virchow's [13] case a dural tumor of some sort was present, but it was not a pial or a ventricular tumor, and therefore we did not include it in our total.

Haverfield and Walker [14] have reported a type of tumor which we rigidly exclude from classification with pial lipomas. Although these authors stated that their tumor and other lipomatous meningiomas do not differ from the lipoma outside the central nervous system, our opinion is to the contrary, and the histologic study of their own tumor contradicts them. They reported that portions of their tumor were composed of meningotheliomatous cells—certainly not to be found in the ordinary lipoma. We have had experience with meningiomas of this sort and though many of the cells may be fatty, even to the point of resembling the cells of adult adipose tissue, the true nature of the tumor is indicated by the presence of sheets of nonadipose cells and whorl-like formations. The most striking gross distinction between fatty meningioma and true lipoma is the lack of dural attachment in the lipoma. True lipoma of the nervous system is similar to lipomas outside the nervous system except that it frequently displays calcification, or even bone.

The 69 cases we found in our partial review of the literature and the 2 cases reported in this communication bring the total to 71 reported cases. Krainer chose to relate the tumors he studied to the various intracranial cerebrospinal fluid cisterns. Though this method of investigation was pertinent to the development of his thesis, the problem seems clearer to us if 70 of the tumors are tabulated according to the structure from which they arose, with the following result: Twenty-five arose from the corpus callosum; 18, from the ventral diencephalic structures; 9, from the choroid plexus or the walls of the lateral and third ventricles; 7, from the dorsal portion of the midbrain; 1, from the ventral portion of the midbrain; 4, from the medulla; 4, from the pons and structures of the cerebellopontile angle, and 2, from the cerebral convexities. Six of the tumors which arose from the corpus callosum were accompanied by one or more additional tumors of the choroid plexus, and 1 was accompanied by a tumor of the olfactory nerve.

One of us, with Love,[1b] has discussed in some detail the problem of the origin of lipoma of the pia mater in connection with intraspinal lipoma; since the problem which concerns lipoma of the brain is the same, it will be adequate merely to list the various mechanisms suggested to account for such a fatty mass. They are: (1) proliferation of the few fat cells normally present in the leptomeninges; (2) deposition of fat in cellular masses arising from proliferation of common connective tissue cells; (3) deposition in connective tissue or glia of fatty products of the breakdown of nerve tissue; (4) fatty degeneration of proliferated glia; (5) abnormal inclusion of fat-forming material within the closing lips of the neural groove, and (6) perverted differentiation of persisting embryonic meninx.

Scherer amplified the last-mentioned mechanism by indicating the probable primitive cells responsible for the formation of the fat—an adaptation of Wassermann's [15] researches. One of us, with Love,[1b] has further amplified this mechanism by suggesting that the primitive cells with fat-forming potentialities are permitted to form fatty masses by a defect in the neural crest. This fundamental defect results in failure of local control of formation of fat, and the stage is set for the lipoma to develop.

The gross and microscopic features of pial lipoma are not significantly different from those of lipoma in other locations except that intracranial lipoma may contain calcified material ranging from psammoma bodies to true bone. In case 1 of this report calcification was present even in the brain substance adjacent to the tumor. The significance of this observation is unknown. An intraspinal pial lipoma containing calcium has not been discovered.[1b]

The clinical importance of the intracranial pial lipoma remains slight even with the demonstration that a tumor of this type may produce symptoms, give roentgenographic evidence of a confusing nature and be subjected to removal. The lesion is merely to be remembered in the differentiation of calcified tumors of the brain.

SUMMARY AND CONCLUSIONS

In 1 of 2 cases of lipoma of the brain described in this paper the tumor caused symptoms of brain tumor, contained enough calcium to cast a shadow in the roentgenogram and was removed surgically.

13. Virchow, R.: Ein Fall von bösartigen, zum Theil in der Form des Neuroms auftretenden Fettgeschwülsten, Virchows Arch. f. path. Anat. **11**:281-288 (March) 1857.

14. Haverfield, W. T., and Walker, A. E.: Lipoblastic Meningioma, Arch. Surg. **42**:371-378 (Feb.) 1941.

15. Wassermann, F.: Die Fettorgane des Menschen. Entwicklung, Bau und systematische Stellung des sogenannten Fettgewebes, Ztschr. f. Zellforsch. u. mikr. Anat. **3**:235-328, 1926.

With the 2 cases reported in this paper, 71 cases of lipoma of the brain or intradural cranial nerves have been reported in the literature. The favored sites of origin, in their order of frequency, are the corpus callosum, the ventral diencephalic structures, the choroid plexus or ventricular walls of the lateral and third ventricles and the dorsal surface of the midbrain.

The mechanism of formation of this lipoma is probably a perversion of differentiation of the primitive meninges. Elements with fat-forming potentialities are present in the meninges, and the lipoma develops when the ectodermal mesenchyme contributing to the leptomeninges is defective.

This tumor has slight clinical importance, but it must be added to the list of lesions requiring differentiation when calcium is discovered on roentgenologic examination.

The Mayo Clinic.

BROMINE CONTENT OF THE BLOOD IN MENTAL DISEASES

I. DEMENTIA PRECOX

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Bromide therapy has been used for many years in the treatment of conditions associated with psychomotor disturbance and increased vasomotor irritability. From time to time the bromide content of the blood of patients with such disorders has aroused the interest of investigators. In 1931 Zondek and Bier [1] reported that in 29 of 34 patients with manic-depressive psychoses who were examined the bromine content of the blood was from 40 to 60 per cent below the normal value (1 mg. per hundred cubic centimeters) previously established by them. The average value for the 34 patients was 0.572 mg. per hundred cubic centimeters. They also stated that in 5 out of 17 patients with schizophrenia studied the blood bromides were low. In 1933 the same authors [2] concluded that the bromide content of the blood of patients with mental disease was likely to be low and discussed the concentration for 6 mentally depressed patients.

Klimke and Holthaus [3] presented the cases of 6 patients with psychomotor disturbances and concluded that lowering of the blood bromides was characteristic and proportional to the intensity of the disturbance. Sacristan and Peraiata [4] analyzed the blood of 13 women with manic-depressive psychoses and in every case found the bromine content to be less than the accepted normal. Ten women with other psychoses were also studied, but no deviation from normal values for blood bromide was noted. On the basis of these results, these investigators concluded that the bromide concentration of the blood was lowered in patients with manic-depressive insanity. Since all these investigators had used methods which were later shown to be unreliable, the validity of their conclusions is open to question.

In 1933 Hennelly and Yates,[5] using a new and more accurate method of analysis of their own, obtained low values for the bromine of the blood for males with schizophrenia of all types, paraphrenia, manic-depressive psychoses and involutional melancholia, while the values for patients with psychoneuroses and organic dementia were within the normal range. These investigators placed little reliance on the estimation of the bromine content of the blood in the diagnosis of manic-depressive psychosis, since no correlation between the stage of the mental disease and variation in the bromine content of the blood could be obtained. These observations were based on the study of 56 patients, including 11 mentally normal patients, as well as the patients with mental disease noted.

Meier and Schlientz [6] used the method of Leipert for the analysis of blood bromides for 35 patients with psychoses. For 27 patients with nonbromide medication the bromine content ranged from 75 to 233 micrograms per hundred cubic centimeters, with an average value of 132 micrograms. Pierre and Camille Chatagnon,[7] also reporting in 1936, stated that for 23 of 31 patients with manic-depressive psychosis which they had studied the bromine values were higher than normal.

Because of the unreliability of the methods used by some of the previous investigators, and because of the few cases of any one type of mental condition included in the reports of any of these workers, we decided to make an extensive study of the bromine content of the blood of various types of mentally disturbed patients. The first investigation was restricted to patients with dementia precox. The subjects chosen had all

From the Department of Physiological Chemistry, Ohio State University College of Medicine.

The present investigation was made possible through the staff of the Columbus State Hospital for the Insane, Dr. J. F. Bateman, Superintendent.

1. Zondek, H., and Bier, A.: Brom im Blute bei manisch-depressivem Irresein, Biochem. Ztschr. **241**: 491, 1931.

2. Zondek, H., and Bier, A.: Brom in Blute bei Psychosen, Klin. Wchnschr. **12**:55, 1933.

3. Klimke, W., and Holthaus, B.: Ueber den Bromspiegel des Blutes bei psychomotorischen Erregungszuständen, Deutsche med. Wchnschr. **58**:1558, 1932.

4. Sacristan, J. M., and Peraiata, M.: Ueber den Bromspiegel des Blutes bei manisch-depressivem Irresein, Klin. Wchnschr. **12**:467, 1933.

5. Hennelly, T. J., and Yates, E. D.: Blood Bromine in the Psychoses, J. Ment. Sc. **81**:173, 1935.

6. Meier, C. A., and Schlientz, W.: Neure Untersuchungen über den Bromspiegel im Blut bei Psychosen, Klin. Wchnschr. **15**:1845, 1936.

7. Chatagnon, P., and Chatagnon, C.: Le métabolism du brome dans l'organism humain, Compt. rend. Acad. d. sc. **202**:1119, 1936.

been inmates of the Columbus State Hospital for the Insane for more than three months, while some had been in residence there for more than ten years.

A method of bromine analysis previously devised by one of us (H. L. W.)[8] was used in this investigation. The accompanying table gives the results for 172 patients with dementia precox.

Although the values in the table range from 0.09 to 1.60 mg. of bromine per hundred cubic centimeters of whole blood, nevertheless the values in few cases approached these limits. The figures for 80 per cent of the subjects differing from this value by less than 0.2 mg. per hundred cubic centimeters. The bromine content of the blood of patients with dementia precox included in the present study therefore appears to be consistently lower than that of normal healthy persons residing in the same geographic area. Differences in blood bromine content of the two groups cannot be attributed entirely to differences in bromide intake in food or water, since the same sources were available to the two groups.

Bromine Content of the Blood of One Hundred and Seventy-Two Patients with Dementia Precox

Case No.	Age, Yr.	Bromine per 100 Cc. Whole Blood	Case No.	Age, Yr.	Bromine per 100 Cc. Whole Blood	Case No.	Age, Yr.	Bromine per 100 Cc. Whole Blood	Case No.	Age, Yr.	Bromine per 100 Cc. Whole Blood
Males			Males			Males			Males		
1	63	0.55	45	37	0.56	89	24	0.49	133	22	0.56
2	60	0.45	46	25	0.36	90	59	0.52	134	59	0.69
3	63	0.58	47	57	0.77	91	40	0.47	135	39	0.40
4	65	0.41	48	35	0.50	92	45	0.62	136	39	0.69
5	75	0.77	49	32	0.38	93	59	0.54	137	24	0.68
6	54	1.00	50	30	0.79	94	55	0.51	138	34	0.68
7	61	0.72	51	34	0.54	95	28	0.56	139	66	0.76
8	77	0.69	52	33	0.42	96	50	0.59	140	50	0.75
9	40	0.56	53	33	0.46	97	27	0.65	141	56	0.48
10	59	0.73	54	35	0.09	98	34	0.52	142	31	0.64
11	48	0.71	55	32	0.56	99	37	0.47	143	35	0.69
12	62	0.59	56	32	0.59	100	37	0.50	144	22	0.47
13	58	0.79	57	32	0.54	101	31	0.60	145	29	0.58
14	55	0.69	58	34	0.38	102	40	0.36	146	64	0.57
15	49	0.43	59	36	0.32	103	33	0.79			
16	45	0.53	60	40	0.56	104	29	0.23			
17	56	0.75	61	62	0.29	105	37	0.67	Females		
18	59	0.69	62	27	0.60	106	52	0.57			
19	46	0.67	63	36	0.55	107	23	0.72	1	62	1.00
20	53	0.36	64	27	1.00	108	44	0.37	2	40	0.50
21	57	0.49	65	47	0.70	109	27	0.45	3	50	0.69
22	47	0.73	66	75	0.70	110	59	0.14	4	32	0.33
23	45	0.59	67	47	0.73	111	29	0.65	5	42	0.56
24	70	0.50	68	30	0.66	112	20	0.54	6	26	0.33
25	50	0.48	69	19	0.39	113	17	0.45	7	35	0.42
26	56	0.63	70	37	0.60	114	31	0.43	8	36	0.35
27	47	0.52	71	46	0.71	115	42	0.79	9	33	0.45
28	49	0.76	72	46	0.79	116	21	1.60	10	34	0.36
29	57	0.18	73	32	0.44	117	37	0.68	11	38	0.93
30	42	0.42	74	30	0.69	118	27	0.58	12	43	0.41
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8. Wikoff, H. L.; Bame, E., and Brandt, M.: A Method for the Determination of Bromine in a Protein-Free Filtrate, J. Lab. & Clin. Med. **24**:427, 1939.

9. Wikoff, H. L.; Brunner, R. A., and Allison, H. W.: The Normal Bromine Content of the Blood of Healthy Individuals, Am. J. Clin. Path. **10**:234, 1940.

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SKULL DEFECT AND HERNIATION OF CEREBRUM WITH ABSENCE OF DURA FOLLOWING HEAD INJURY IN ADOLESCENCE

CAPTAIN WILLIAM S. McCUNE
AND
MAJOR BARNES WOODHALL
MEDICAL CORPS, ARMY OF THE UNITED STATES

A few cases of delayed absorption in bones of the skull following head injury have been described. Pancoast, Pendergrass and Schaeffer [1] reported a case in which an unusual alteration in bony structure developed after a fracture of the skull, with hernia of the cerebrum and elevation of a fragment of bone from the cranium. Rowbotham [2] described a defect in the vault of the skull with traumatic malacia or absorption of bone following a closed head injury. The thinning and scalloping of bone adjacent to a comminuted fracture of the skull, characteristic of traumatic cyst of the leptomeninges, is not unusual. It was well portrayed by Dyke [3] and has been duplicated in our series of head injuries. However, in a review of the literature we have been able to find no instance of a defect in the inner table of the skull alone with herniation of the brain and absence of dura mater following head injury. Having encountered such a case, we present it as an aid in the differentiation of lesions of this type from tumors and infections of the skull.

REPORT OF A CASE

History—A private in the Women's Army Corps, aged 32, was admitted to the Walter Reed General Hospital on Feb. 10, 1944, as a transfer from the station hospital at Fort George G. Meade, Md., because of headache, fainting spells and the presence of an irregular area of destruction of bone in the left parietal area of the skull.

She stated that at the age of 15 (in 1927), while walking along a country road one evening, she had been knocked down by a passing automobile, which struck the left side of her head. She was unconscious for twenty or thirty minutes. She received medical care and was kept in bed for two weeks, but no roentgenograms of the skull were taken. Except for mild, transient frontal headaches, she was well after the accident until 1939. During that year headaches, which were not lateralized and not accompanied by vomiting, became more severe and recurred two or three times a month, each attack lasting about twelve hours. Under a regimen of rest the attacks subsided again, only to recur in 1943, after she had enlisted in the Women's Army Corps. In November 1943, one month after enlistment, she felt dizzy one day while marching to a class and fainted on reaching the school where the classes were held. She did not have a convulsion and was unconscious for only five minutes. Later in the same month, while drilling, one day, she fainted again, and she had two similar episodes on Jan. 17 and Jan. 18, 1944, without convulsive movements, biting of the tongue or incontinence. Examination at the Fort George G. Meade Station Hospital revealed only an equivocal Babinski sign on the right side. Because of the finding of an irregular defect in the left parietal bone, however, she was transferred to the Walter Reed General Hospital for further study, arriving there on February 10.

Examination.—Physical examination on admission to the hospital revealed no evidence of acute disease. There was slight tenderness over the left parietal area of the skull on tapping or pressure. The blood pressure was 110 systolic and 76 diastolic. General physical examination revealed nothing abnormal except for a small mass in each pelvic vault. Neurologic examination showed no significant abnormalities.

Roentgenograms of the skull revealed an area of moth-eaten destruction in the left parietal bone, beginning close to the sagittal suture line and extending laterally in the midparietal area for a distance of about 7 cm. (figure, *A*). The anteroposterior diameter was about 4.5 cm., and in the posteroanterior projection the volume of the skull seemed larger on the left side. The inner table alone appeared involved in the diffuse destructive process. There was no increased vascularity in the surrounding bone and no definite involvement of the scalp. The roentgenographic impression was that of cholesteatoma of the left parietal bone. Roentgenograms of the long bones, the pelvis and the thoracic cage showed no abnormalities.

An electroencephalogram recorded a dominant rhythm of 10 per second. There were no seizure discharges and no evidence of a focal lesion. Overventilation pro-

From the Neurosurgical Section, Walter Reed General Hospital, Washington, D. C.

1. Pancoast, H. K.; Pendergrass, E. P., and Schaeffer, J. P.: The Head and Neck in Roentgen Diagnosis, Springfield, Ill., Charles C Thomas, Publisher, 1940.

2. Rowbotham, G. F.: Acute Injuries of the Head, Edinburgh, E. & S. Livingstone, 1942.

3. Dyke, C. G.: The Roentgenological Aspects of Fracture of the Skull and Injuries to the Brain, in Brock, S.: Injuries of Skull, Brain and Spinal Cord, ed. 2, Baltimore, Williams & Wilkins Company, 1943.

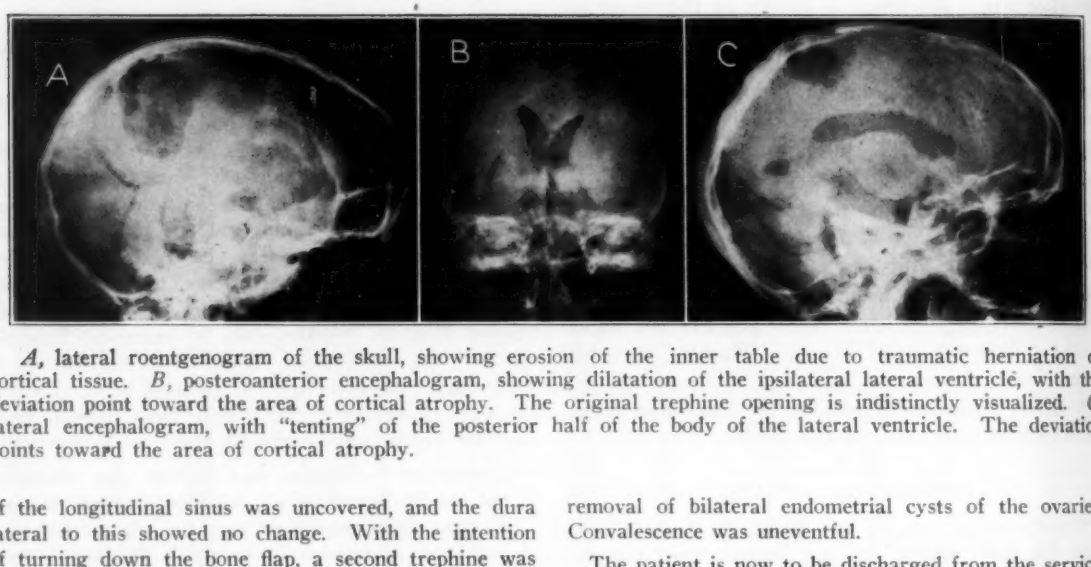
duced no increased frequency of potentials. The impression was that of a normal electroencephalogram. A spinal puncture showed normal pressure, no cells and a total protein of 25 mg. per hundred cubic centimeters.

Operation.—On February 22, with the patient under ether anesthesia administered intratracheally, a small flap was marked out on the left parietal region of the scalp, with its base along the midline. A small linear scar, apparently the result of the old head injury, was situated in the center of a small depression palpable in the parietal bone. The flap of the scalp was reflected and bleeding controlled with Raney clips. The pericranium was left intact, and there was no scarring in this plane of the scalp. Beginning at the midline, the pericranium was reflected laterally for a distance of 2 or 3 cm. This disclosed an old comminuted fracture of the parietal bone. A trephine opening was made in the caudal and mesial aspect of the operative defect through one of the old fracture lines. Nothing was seen through the thickness of the bone. About 3 mm. of the longitudinal sinus was uncovered, and the dura lateral to this showed no change. With the intention of turning down the bone flap, a second trephine was made rostrally in the same plane. When this had been carried through the bone for a distance of 3 mm., a round, irregular hole, measuring 2 or 3 mm. in diameter, presented on the lateral aspect of the trephine opening. The tip of a forceps passed through this hole encountered no resistance, and the tissue protruding through it was obviously cortical. The trephine opening was carried along cautiously; again, on its lateral aspect another large defect in the bone appeared, and, again, cortical tissue presented. Examination of a frozen section showed normal brain tissue. It seemed evident, then, that a bone flap could not be turned down without destroying a large part of this apparent herniation of cortical tissue. The trephine openings were therefore filled with bone dust, and the scalp flap was resutured with fine silk sutures through galea and scalp.

Postoperative Course.—On the afternoon following operation there developed right hemiparesis, more pronounced in the lower extremity, with increased reflexes and a positive Babinski sign on the right side. There was no aphasia. The patient complained of numbness of her right arm and leg, but careful neurologic examination showed no sensory loss. An electroencephalogram made on Feb. 29, 1944, revealed potentials of moderately decreased amplitude over the entire left hemisphere, but a second examination, on March 11, showed no difference in amplitude.

On April 12 pneumoencephalograms (figure, *B* and *C*) demonstrated slight dilatation and upward displacement of the posterior half of the body of the left ventricle. The deviation of the ventricle pointed toward the defect in the skull. It was the opinion of the roentgenographic section that this was indirect evidence of cortical atrophy in the left parietal area of the brain.

Because of abdominal pain and the discovery of the pelvic masses already noted, an exploratory pelvic laparotomy was performed on July 8, 1944, with the removal of bilateral endometrial cysts of the ovaries. Convalescence was uneventful.



A, lateral roentgenogram of the skull, showing erosion of the inner table due to traumatic herniation of cortical tissue. *B,* posteroanterior encephalogram, showing dilatation of the ipsilateral lateral ventricle, with the deviation point toward the area of cortical atrophy. The original trephine opening is indistinctly visualized. *C,* lateral encephalogram, with "tenting" of the posterior half of the body of the lateral ventricle. The deviation points toward the area of cortical atrophy.

The patient is now to be discharged from the service. Her only complaint is mild headache in the left frontal and parietal region and some weakness of the muscles of the right thigh and lower leg. Examination reveals only slight weakness in function of the quadriceps muscle and in dorsiflexion of the right foot.

SUMMARY

The degenerative process in the cranium following fracture of the skull during adolescence in this case was unusual in the destruction of the inner table, the herniation of the brain into the defect and the absence of dura mater over the area of involvement. It is hoped that a description of the findings in this case may aid in the rather difficult differential diagnosis in similar cases in the future.

MYELITIS COMPLICATING MEASLES

LAURENCE A. SENSEMAN, M.D.

SAYLESVILLE, R. I.

Myelitis as a complication of measles is rare. Only 4 cases have been reported in the American literature.[1] Ford [2] reviewed the world literature in 1928 and listed 29 cases of myelitis complicating measles. Rydeen and Glaser [1] found the reports of 8 cases since 1928, most of which are in the European literature. Little is known about the etiology and pathogenesis. Many observers believe that the condition is an acute inflammatory process caused by the neurotropic virus of measles. Finley [3] stated the opinion that allergy plays an important part in the pathogenesis. He based this belief on the fact that the complication appears at the height of the virus-antibody reaction and suggested that the myelitis is the result of a hypersensitive response on the part of the nervous system. Rivers and Schwenkter,[4] working with monkeys, produced a demyelination encephalomyelitis by the repeated intravascular injection of a suspension of rabbit brain. They stated that the character of the lesions observed was such as to suggest that they were caused by an infectious agent. Putnam [5] stated the opinion that the disease is noninfectious and that the fundamental abnormality is a spontaneous thrombosis of the small blood vessels within the central nervous system; he suggested that the abnormality may be basically allergic; i. e., an instability of the blood-clotting mechanism may be one aspect of allergy. Morris and Robbins [6] stated that measles per se is a relatively "simple" disease but that its neurologic complications require further study and interpretation. Because of the rarity with which cases of postmeasles myelitis are reported in the literature, the following case is briefly described.

REPORT OF A CASE

A. M., aged 24, a Naval Air Corps officer, was confined to the house with measles while on leave, on April 10, 1944. On the fourth day following the appearance of the rash the patient attempted to get out of bed and noticed pain and weakness in his legs. The following day he could not walk and complained of backache and headache. He noted that the skin of his legs was very sensitive and that he had a stiff neck. By noon of the same day he was unable to void. At the time of his illness he was in the home of his brother-in-law, a physician, who made a diagnosis of measles and arranged for a neurologic consultation.

Examination revealed a well developed and well nourished man who seemed rather ill. Some rash was still present. The temperature was 100 F.; the pulse rate was 80, and respiration was normal. The patient was perspiring freely. He complained of pains in the lower extremities, bachache and headache. The pupils were equal and reacted normally to light and in accommodation, and the fundi were normal. The cranial nerves were not involved. There was some nuchal rigidity. The deep reflexes were all of 4 plus intensity, and the abdominal and cremasteric reflexes were absent. Ankle and knee clonus were present and were more active on the left side than on the right. The Babinski and Hoffmann signs were not elicited. The Romberg test was not attempted because of the patient's condition.

A rather irregular area of hyperesthesis extended from the lower border of the ribs to the level of the umbilicus. Below that level sensation was definitely impaired. Urinary retention was evidenced by distention of the bladder, apparent on percussion. Lumbar puncture was productive of clear spinal fluid, with an initial pressure of 180 mm. Examination of the fluid revealed 3 white cells per cubic millimeter, a normal protein content, and 56 mg. of sugar and 725 mg. of chloride per hundred cubic centimeters. Culture of the fluid yielded no pathogens. The Wassermann reaction was negative.

The patient was transferred at once to a Naval hospital, where laboratory and physical examination gave essentially the same results as those already noted and the diagnosis of postmeasles myelitis was confirmed. Their neurologic study, made on April 14, was reported as follows: "Examination revealed normal cranial nerves; minimal weakness of the legs; absence of abdominal reflexes; an apparent increase in the deep re-

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2. Ford, F. R.: The Nervous Complications of Measles, with a Summary of the Literature and Publication of Twelve Additional Case Reports, Bull. Johns Hopkins Hosp. **43**:140, 1928.

3. Finley, K. H.: Pathogenesis of Encephalitis Occurring with Vaccination, Variola and Measles, Arch. Neurol. & Psychiat. **39**:1047 (May) 1938.

4. Rivers, R., and Schwenkter, F. F.: Encephalomyelitis Accompanied by Myelin Destruction Experimentally Produced in Monkeys, J. Exper. Med. **61**:689, 1935.

5. Putnam, T. J.: Newer Conceptions of Postinfectious and Related Forms of Encephalitis, Bull. New York Acad. Med. **17**:337, 1941.

6. Morris, M. H., and Robbins, A.: Acute Infectious Myelitis Following Rubella, J. Pediat. **23**:365, 1943.

flexes, and an indefinite band of dysesthesia for superficial sensation from the fourth to the sixth thoracic dermatome on the right side and the twelfth thoracic dermatome on the left."

A progress note, on April 20, indicated that the patient was "improving rapidly and had been able to walk with assistance for the past two days." By May 1 he had "no complaints and had been ambulatory for several days." On May 6, twenty-six days after onset, he was "discharged to active duty."

Reexamination, on May 10, 1944, gave the following results: "There was no involvement of the cranial nerves; sensation was entirely normal, but the reflexes were still increased bilaterally, particularly on the left side." The patient stated that while he had slight pain in the back, he was still able to carry out his usual routine duties in the Navy. Since then, and up to Dec. 27, 1944, the patient has been on full active duty. He has lost no time because of illness.

SUMMARY

Because of the rarity with which postmeasles myelitis is reported in the literature, a case is briefly described, in which no specific therapy was instituted and the patient recovered, without residuals.

160 Chapel Street.

Case Reports

DISPLACEMENT OF THE PINEAL GLAND WITH EXTRADURAL HEMORRHAGE

M. J. Madonick, M.D., and Ignaz W. Oljenick, M.D., New York

Although displacement of the pineal gland in cases of intracranial hemorrhage [1] and subdural hematoma [2] has been described, mention of such an occurrence with extradural hemorrhage is uncommon in the literature.

We report the following case of shift of the pineal gland with epidural bleeding due to traumatic rupture of the middle meningeal artery.

REPORT OF A CASE

E. M., a Negro aged 40, was admitted to the Morrisania City Hospital in a comatose state at 5:10 a. m. on Dec. 1, 1944. He had been found unconscious in a subway station. No further information was obtainable.

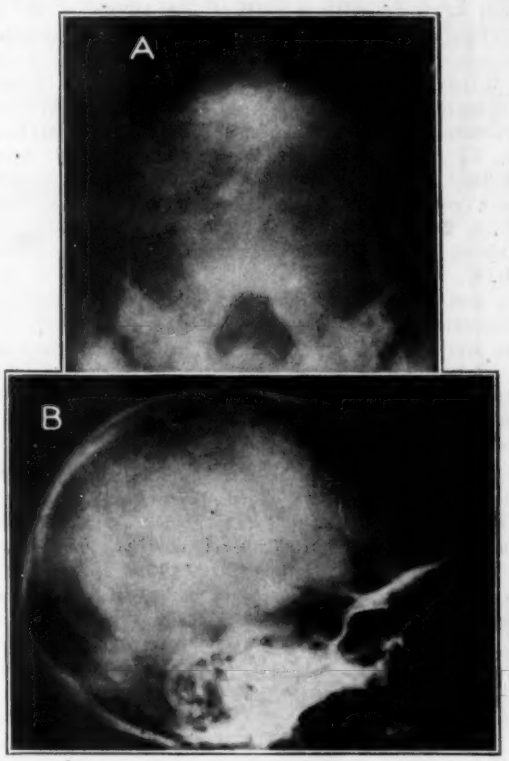
Examination on his admission to the ward revealed that he was well developed and well nourished. The pulse rate was 44 per minute, the temperature 95 F., the respiratory rate 12 per minute and the blood pressure 100 systolic and 65 mm. diastolic. There was a bruise over the left temporal region. His breath had an alcoholic odor. He was unconscious but moved his limbs on heavy supraorbital pressure. The left pupil was much larger than the right and was fixed to light; the right pupil reacted to light. The deep reflexes were hyperactive on the right side, and there were a positive Hoffmann sign and an inconstant Babinski sign on that side. Spinal tap disclosed grossly bloody fluid, which did not clear. A cell count showed 40,000 crenated erythrocytes per cubic millimeter.

At 10 a.m., five hours after his admission, the patient was still comatose but moved his limbs on stimulation of the nasal mucosa. The left pupil was fully dilated, and the right had dilated to nearly the same size as the left; neither pupil reacted to light. There was no papilledema. Meningeal signs were not elicited. There was slight eversion of the left lower limb, with a Babinski sign on the same side. The deep reflexes were depressed throughout.

The blood sugar was 118 mg. and the urea nitrogen 16.5 mg. per hundred cubic centimeters, and the Kahn reaction of the blood was negative. Urinalysis revealed nothing abnormal.

Roentgenographic study of the skull showed a linear fracture line in the left temporal region which entered the base of the skull and crossed the groove of the middle meningeal artery (figure, *B*). The pineal gland was displaced 1 cm. to the right of the midline, 1 cm. posteriorly and 0.5 cm. downward (figure, *B*), as observed by the method of Vastine and Kinney.[1a]

Operation was performed with infiltration of a solution of procaine hydrochloride containing epinephrine hydrochloride. An exploratory burr hole was made over the site of the fracture line. Dark blood was seen as soon as the opening was completed. An osteoplastic flap was turned down. A large clot, estimated to contain about 500 cc. of blood, was evacuated, and the ruptured middle meningeal artery was clipped. The brain did not show any tendency to return to its normal place. On the patient's return to the ward his condition was unchanged.



Roentgenograms showing (*A*) lateral and (*B*) downward and posterior displacement of the pineal gland. A fracture line is seen crossing the groove of the middle meningeal artery.

The patient did not recover consciousness. The respiratory rate rose to 40 per minute and the temperature to 104 F., and bronchopneumonia developed. He died three days after operation. Autopsy, by the medical examiner, revealed a fracture, as noted in the roent-

From the Neurologic Service of Dr. N. Savitsky, Morrisania City Hospital.

1. (*a*) Vastine, J. H., and Kinney, K. K.: The Pineal Shadow as an Aid in the Localization of Brain Tumors, Am. J. Roentgenol. **17**:320, 1927. (*b*) Naffziger, H. C.: Method for the Localization of Brain Tumors, Surg., Gynec. & Obst. **40**:481, 1925.

2. Dyke, C. G., and Davidoff, L. M.: Chronic Subdural Hematoma: A Roentgenographic and Pneumencephalographic Study, Bull. Neurol. Inst. New York **7**:112, 1938. Pancoast, H. K.; Pendergrass, E. P., and Schaeffer, J. P.: The Head and Neck in Roentgen Diagnosis, Springfield, Ill., Charles C Thomas, Publisher, 1942, p. 637. Lauder, G. H.; Browder, E. J., and Watson, R. A.: Subdural Hematoma, Ann. Surg. **113**:170, 1941. Gross, S. W., and Ehrlich, W.: Diagnosis and Treatment of Head Injuries, New York, Paul B. Hoeber, Inc., 1940, p. 55.

genogram, and a small quantity of extradural blood. Examination did not reveal subdural effusion, brain tumor or edema of the left hemisphere.

The literature dealing with roentgenologic findings in the skull in cases of extradural hemorrhage is chiefly concerned with the presence or absence of a fracture line crossing the groove of the middle meningeal vessels. Although in occasional cases such a fracture is not present,[3] the majority of authors have stated the opinion that it always exists.[4] In fact, Eynon [4c] favors trephination in all cases in which such a fracture is shown even though there are no symptoms. Mehrtens and Newell [5] described the case of a man aged 52 with a shift of the pineal gland of 0.5 cm., which returned to its position in the midline about eight weeks after an acute head injury. Their diagnosis was cerebral contusion. Schüller,[6] in a discussion of acute head injuries, stated:

> The diagnosis of an extensive hemorrhage inside the cranial cavity can be made if a displacement of the pineal shadow is present.

However, he did not describe the type of hemorrhage or its location. The only reported case that we find in which there was a shift of the pineal body with extradural bleeding was the first case reported by Falconer and Schiller,[3a] that of a man aged 30 with slight displacement of the gland. The patient recovered after operation. In Grant's [7] case a lateral view of the skull showed a slight shift of the pineal gland posteriorly, but, unfortunately, the pineal shadow was not seen in the anteroposterior view.

CONCLUSION

Displacement of a calcified pineal gland in a case of extradural hemorrhage was demonstrable in a roentgenogram. We have been able to find only 1 similar instance in the literature. We believe that a large effusion of blood must be present to produce the shift. In cases of acute head injury attention should be directed not only to the presence of a fracture line but to displacement of the pineal gland. The case described demonstrates that such a shift can be caused by extradural hemorrhage, and not by subdural or intracerebral bleeding only.

1882 Grand Concourse.

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3. (*a*) Falconer, M. A., and Schiller, F.: Middle Meningeal Haemorrhage After Head Injury Without Fracture of the Skull, Lancet **1**:532, 1942. (*b*) McKenzie, K. G.: Extradural Haemorrhage, Brit. J. Surg. **26**:346, 1938. (*c*) Turner, J. W. A.: Observations on the Cerebrospinal Fluid in Closed Head Injuries, Brit. M. J. **2**:569, 1941. (*d*) Jacobson, W. H. A.: On Middle Meningeal Haemorrhage, Guy's Hosp. Rep. **43**:147, 1886. (*e*) Woodhall, J. W.; Devine, J. W., Jr., and Hart, D.: Fractures and Other Trauma—Homolateral Dilatation of the Pupil, Homolateral Paresis and Bilateral Muscular Rigidity in the Diagnosis of Extradural Hemorrhage, Surg., Gynec. & Obst. **72**:391, 1941. (*f*) Amyot, R.: Hémorragie extradurale par rupture traumatique de la méningée, Union méd. du Canada **69**:485, 1940.

4. (*a*) Peet, M. M., in Brock, S.: Injuries of the Skull, Brain and Spinal Cord, Baltimore, Williams & Wilkins Company, 1940, p. 133. (*b*) Munro, D., and Maltby, G. L.: Extradural Hemorrhage: A Study of Forty-Four Cases, Ann. Surg. **113**:192, 1941. (*c*) Eynon, C. M.: A Case of Symptomless Middle Meningeal Haemorrhage, Canad. M. A. J. **16**:957, 1926.

5. Mehrtens, H. G., and Newell, R. R.: Displacement of the Pineal Gland in Head Injury, J. Neurol. & Psychopath. **6**:198, 1925.

6. Schüller, A.: X-Ray Examination in Recent Head Injuries, M. J. Australia **1**:641, 1941.

7. Grant, W. T.: Chronic Extradural Hematoma: Report of a Case of Hematoma in Anterior Cranial Fossa, Bull. Los Angeles Neurol. Soc. **9**:156, 1944.

Obituaries

LLOYD HIRAM ZIEGLER, M.D.
1892-1945

Dr. Ziegler, medical director of the Milwaukee Sanitarium, Wauwatosa, Wis., died there, in the midst of his work, the evening of Jan. 8, 1945. Death came in a coronary heart attack, shortly after supper, as he was about to interview a patient. There had been no previous attack. Dr. Ziegler was a man of great energy and drive; he pursued his hobbies with as much intensity as he did his professional work. As a result, relaxation did not come easily to him; action was his life, and in action he died, at the age of 52.

(Photograph by Blackstone Studios, 20 West Fifty-Seventh Street, New York.)

LLOYD HIRAM ZIEGLER, M.D.
1892-1945

He was born in Bippus, Ind., June 1, 1892. His education and training were broad. He received his Bachelor of Arts and his Master of Arts in psychology from Indiana University in 1914 and 1916, and his Doctor of Medicine from the University of Minnesota in 1921. His internship was served at St. Elizabeths Hospital, Washington, D. C., after which he entered the United States Public Health Service, working with the veterans of the First World War, before the Veterans Administration became a separate organization. He then became house officer at the Phipps Psychiatric Clinic under Adolf Meyer, whose thoughts and comments remained deeply etched in his memory. There followed a fellowship in neurology at the Mayo Clinic and a year as resident at the Colorado Psychopathic Hospital, in Denver.

Dr. Ziegler then returned to the Mayo Clinic in 1926 as a member of the staff of the section on neurology and remained there until 1930, when he took charge of the department of neurology and psychiatry at Albany Medical College and the Albany Hospital. At Albany he plunged into a strenuous program of teaching, administration and clinical work, the last including not only his activities in connection with the school and hospital but an active private consulting practice.

In 1937 Dr. Rock Sleyster, director of the Milwaukee Sanitarium, asked Dr. Ziegler to come to Wauwatosa as his associate director. He did so, and on Dr. Sleyster's death, in March 1942, he succeeded him as medical director.

Dr. Ziegler's professional life was one of unremitting labor. This is partly attested to by the long series of his publications in neurology and psychiatry. At the time of his death he was at work on a book which was to deal with his basic ideas on the problem of human behavior and its deviations, for which he had collected a great deal of historical and technical material. Several chapters had already been written.

In his teaching, which took much of his energy and enthusiasm, he left a deep impression. It was his constant aim to stimulate, encourage and guide, without domineering, and many students and house officers remember his efforts in their behalf.

One of his distinctions, a necessarily rare one, was that of being a founding member of the American Board of Psychiatry and Neurology. He continued to serve on that board, without interruption, until he died. Only a person who has seen something of the tasks and problems of that board—even from the sidelines—can appreciate the amount of mental and physical stress involved in such an assignment.

Dr. Ziegler was profoundly aware of his duties as a citizen and was alert to the problems of government and social organization. One of these problems, with which he had had early experience, was that of the returning veteran. And one of his last activities in this field was his initiative in the establishment of a voluntary neuropsychiatric rehabilitation clinic in Milwaukee, under the auspices of the Neuro-Psychiatric Association there. Ironically, he was never able to attend that clinic. His duties on the American Board kept him away the night it opened; he had planned to come the evening he died, but a clinical responsibility intervened then also. He was active in the cause of mental hygiene and made many addresses furthering public interest in it.

No account of Dr. Ziegler's work would be complete without a mention of his closest collaborator, his wife. She shared the work in every paper he wrote, editing and transcribing, and to her he confided his notes and his ideas about the book he was writing. A closer working partnership cannot be imagined than existed between these two. He is survived by her and by his brother, Major Newell Ziegler, also a physician, and a sister, Mrs. Leland Rogers.

Dr. Ziegler was a member of many professional societies and committees, and of Phi Beta Kappa, Sigma Xi and Alpha Omega Alpha. He was less interested in the political aspects of his societies than in their medical, scientific and humanitarian activities, and he was always eager to further these objectives.

Above all, and more important than his outstanding gifts of intellect, energy and kindness, was the fact of his uncompromising integrity, a quality without which all other endowments, in a physician especially, are worse than worthless. In Dr. Ziegler's passing members of the medical profession and the public have lost a true physician and a true man, one who has left his mark not only in his written words but in the memories of those who knew him.

JOSEF A. KINDWALL, M.D.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

EMBRYONIC GRAFTS IN REGENERATING TISSUE: II THE BEHAVIOR OF THE TRANSPLANTS DURING HOST METAMORPHOSIS IN RANA PIPIENS. HENRY S. EMERSON, J. Exper. Zool. **95**:61 (Feb.) 1944.

Grafts of the embryonic eye and adjacent tissues (Rana pipiens) differentiate well in the larval tail blastema and continue to live long after the tail is fully regenerated. The eye, with lens; brain parts, and striated muscle may live over ninety days, and cartilage over one hundred days, after operation, an observation which indicates indefinite existence in this environment.

Some of the transplants disintegrate after the first week or two of differentiation. The frequency of this necrosis does not depend on the length of time in the host. Often all the graft is resorbed except the cartilage.

During the first half of the period of resorption of the host tail the transplants are not affected, but during the last half of this period most of them are resorbed. This is due to difficulties in successful transfer of the graft from the tadpole tail to the body of the young frog. After metamorphoris the transplant tissue may remain in the posterior end of the host, or, more rarely, a large graft is retained near the tip of the urostyle of the young adult frog.

Large transplants present after metamorphosis are still covered by host epidermis, originally skin of the tadpole tail. Apparently, the graft must prevent the skin of the larval tail from being resorbed. However, this epidermis approaches in coloration, degree of cornification and character of the cutaneous glands the skin of the adult body.

REID, Boston.

METHODS OF INITIATING LIMB REGENERATION IN ADULT ANURA. S. MERYL ROSE, J. Exper. Zool. **95**:140 (March) 1944.

After limb amputation, the limb stumps of adult frogs (Rana clamitans, Rana palustris and Rana pipiens) healed rapidly, with a covering of old skin. There was no regeneration except that of cartilage and skin and the formation of scar tissue. When amputation surfaces remained open because of treatment with strong salt solutions or because the skin was cut away or for some other reason, regeneration began. Regeneration of a normal distal forearm and wrist region was obtained in sodium chloride–treated frogs when the amputation was made through the midforearm. The regenerants were all abnormal in the hand region.

The author discusses at length the manner in which skin may inhibit regeneration. The treatments that evoke latent regenerative ability are drastic and may act by causing removal or dedifferentiation of inhibiting skin or by producing internal trauma, with consequent hyperemia, edema and dedifferentiation. The barrier blocking better regeneration of the frog limb appears to be early development of the dermis and fibrous scar tissue.

REID, Boston.

FURTHER EXPERIMENTAL EVIDENCE AGAINST "NEUROTROPISM" IN NERVE REGENERATION. PAUL WEISS and A. CECIL TAYLOR, J. Exper. Zool. **95**:233 (March) 1944.

No deflection of nerve fibers toward degenerating nerve has been observed in tissue culture, either in blood plasma or in liquid medium.

Sciatic nerves in the rat were allowed to regenerate in forked arteries (bifurcation of the abdominal aorta into the two common iliac arteries). The outgrowing fibers were confronted with alternative routes, either into blind channels or into channels containing degenerated nerve, tendon or fat tissue. Nerve fibers grew into blind channels with the same density and orientation as into channels containing degenerated nerve. Supposedly, "neurotropic" agents in one channel did not deflect nerve fibers in that direction. There was no tendency for nerve fibers approaching the entrance of a channel containing degenerated nerve to converge on it.

Nerve fibers in a blind channel formed irregular terminal plaques. Although there was no functional connection with appropriate end organs, these plaques persisted, without signs of resorption, for at least twenty weeks. In a single case fibers connected with a functional periphery grew to a larger size (diameter) than did unconnected fibers.

REID, Boston.

NEURAL DIFFERENTIATION OF ECTODERM THROUGH EXPOSURE TO SALINE SOLUTION. JOHANNES HOLTFRETER, J. Exper. Zool. **95**:307 (April) 1944.

The hypothesis of Barth that isolated ectoderm of an early amphibian gastrula when curled up in a favorable direction will form neural tissue was tested by corresponding explantations performed on the different areas of gastrulas of Triturus torosus and Amblystoma punctatum.

Pure ectoderm of T. torosus, cultured in saline solution, did not develop neural tissue. Irrespective of the initial curling, presumptive medullary plate and presumptive epidermis formed merely epidermis. These results confirm the generally accepted view.

Isolated ectoderm of A. punctatum differentiated into neural tissue in 60 per cent of the gastrulas. However, there was no indication that the early gastrula ectoderm is endowed with a gradient for neural formation or that the initial curling is causally related to the trend of differentiation.

Explants from gastrulas in more advanced stages showed a higher percentage of cases of neural formation when taken from the presumptive medullary plate (100 per cent) and a lower percentage when taken from the presumptive epidermis (15 per cent). Determinative stimuli must be received by the ectoderm from invaginated tissues before the time of isolation.

In explants of A. punctatum prolonged exposure to saline solution produces peripheral disintegration of the uncoated ectoderm cells. The quantity and location of neural tissue within an explant can be correlated with the proportional amount and the site of decomposition. The inductive effect of the medium may result from

stimuli from the decaying free cells or from a less severe denaturation of the surviving cells themselves.

Whenever the amount of induced neural tissue reached a certain volume, it became organized into a brainlike structure. Eyes, nasal placodes and, in rare cases, derivatives of the neural crest could be formed by any area of the gastrula ectoderm. The axial polarity of these formations was influenced by their topographic relation to the source of induction.

REID, Boston.

RESTITUTION OF THE MEDULLA FOLLOWING UNILATERAL EXCISION IN THE EMBRYO. S. R. DETWILER, J. Exper. Zool. **96**:129 (July) 1944.

Unilateral excision of the medulla in embryos of Amblystoma punctatum with closed neural folds (stages 21 to 23) may be followed by gradual restitution from the contralateral, intact, wall. This restitution is accomplished by extensive proliferation and migration of extraependymal cells of the intact side, and not from the cephalic and caudal stumps on the side of excision. The ependyma does not play any compensatory role in the proliferative processes.

In embryos with bilaterally symmetric medullas, the regenerated wall appears complete and normal except for the absence of Mauthner's cell and the failure of the vestibular system to develop. On the intact side the medial longitudinal fasciculus is slightly reduced in size.

When physiologic failures occurred, such as inability to lurch and snap at food, the medullas were observed to show disorderly and bizarre arrangements of cells and fiber bundles. In embryos with complete regeneration, the physiologic activities were essentially complete except for the limitations imposed by the absence of Mauthner's neuron and the vestibular apparatus.

In embryos with completely closed neural tubes, one-half the medulla is essentially totipotent for the whole.

REID, Boston.

SELECTIVITY OF NERVE FIBERS FROM THE DORSAL AND VENTRAL ROOTS IN THE DEVELOPMENT OF THE FROG LIMB. A. CECIL TAYLOR, J. Exper. Zool. **96**:159 (July) 1944.

The relation of nerve fibers from the dorsal and ventral roots to their terminal tissues in the developing limb bud of the frog (Rana pipiens) was investigated by means of experiments in which the spinal ganglia or portions of the spinal cord were removed at an early larval stage. In the absence of ventral root fibers, no muscular nerves were established, while a typical pattern of cutaneous nerves was produced by the remaining dorsal root fibers. When dorsal root fibers were absent, typical muscular nerves were developed, and, in addition, many small cutaneous nerves were present. Taylor suggests that the fine fibers of the cutaneous nerves may be of sympathetic origin.

A selective action of the nerve fibers results in the termination of nerves in homologous tissue. The selectivity of pioneer fibers is probably one of preneural pathways, rather than of the terminal tissues themselves. Later fibers exhibit selectivity in relation to established neural pathways.

REID, Boston.

CELL NUMBER AND CELL SIZE IN THE ECTODERM DURING NEURULATION (AMBLYSTOMA MACULATUM). ROY GILLETTE, J. Exper. Zool. **96**:201 (Aug.) 1944.

An estimation was made of changes in ectodermal volume, cell number and cell size during neurulation in Amblystoma maculatum. This was done by measuring the cross section areas and by counting nuclei in fixed sections selected at equal intervals along the entire length of 10 neurulas, representing various stages.

An increase of 23 per cent in the number of cells present in the total ectoderm without an increase in total volume of the ectoderm during neurulation indicates that the mitotic activity represents cleavage. An analysis of various regions shows that the decline in cell size is a general feature of all parts of the ectoderm. No significant difference in cell size was observed between the dorsal regions, containing mostly neural tissue, and the lateral and ventral regions, containing epidermal cells.

There is a pronounced gradient in cell size in the anterior-posterior axis of the neurula, with the smaller cells anteriorly. This gradient is present throughout neurulation and is regarded as a manifestation of the animal-vegetal gradient which originated during cleavage stages.

Gillette concludes that localized cell enlargement and differences in mitotic rate are not involved in neurulation up to the meeting of the neural folds. The thickening of the neural plate is attributed to a concentration in the dorsal region of cells from both the lateral and the dorsal areas. The thickening of the neural plate, though to a certain extent autonomous, is part of the general pattern of morphogenetic movements of the entire neurula.

The author suggests that the folding of the plate is a direct result of the contraction process, which progresses at a greater rate at the surface than in the deeper tissues. Thus, the surface coat of Holtfreter may be an important factor in neurulation, as well as in gastrulation.

The interpretation of epithelial expansion and contraction in terms of "surface tendencies" of the cells provides a method for the quantitative analysis of morphogenetic movements occurring in epithelial layers.

REID, Boston.

THE EFFECTS OF PERIPHERAL FACTORS ON THE PROLIFERATION AND DIFFERENTIATION IN THE SPINAL CORD OF CHICK EMBRYOS. VIKTOR HAMBURGER and EUGENE L. KEEFE, J. Exper. Zool. **96**:223 (Aug.) 1944.

Hamburger and Keefe made an analysis of the hypoplasia of the lateral motor columns at the brachial level caused by extirpation of the wing bud in early chick embryos, and of the hyperplasia observed in similar segments of the cord when a supernumerary wing was implanted beside the host wing.

In embryos with unilateral extirpation of the limb there was a slight effect of the operation on the rate of proliferation, as shown by mitotic figure counts made during the peak of activity at the brachial level of the spinal cord. This effect appeared to be transient. Separate cell counts made of the lateral motor and of the nonmotor ventral neurons of the brachial and lumbosacral levels of the cord showed that the total cell numbers were strikingly identical for the two sides in all instances, whether of limb extirpation (4 embryos) or of wing transplantation (1 embryo). The deficit of motor neurons in cases of hypoplasia was balanced by an excess of nonmotor neurons. In the case of motor hyperplasia the surplus was compensated for by a deficit in nonmotor cells. It is concluded that peripheral factors control the differentiation of potential neuroblasts into motor neurons. The mechanism of peripheral control is discussed, and an inductive effect of differentiated

primary motor neurons on adacent indifferent cells is postulated.

In view of these results and of other recent studies, the authors suggest that a similar effect of peripheral factors on differentiation of motor neurons exists also in the urodeles.

REID, Boston.

Physiology and Biochemistry

A STUDY OF GNOSIS, PRAXIS AND LANGUAGE FOLLOWING SECTION OF THE CORPUS CALLOSUM AND ANTERIOR COMMISSURE. ANDREW J. AKELAITIS, J. Neurosurg. **1**:94 (March) 1944.

The purpose of this study was to evaluate the role of the anterior commissure in interhemispheral connections after partial or complete section of the corpus callosum. The tests used toward this end included observations on body laterality, a study of the higher visual functions in each homonymous field, praxis, auditory gnosia, tactile gnosia, temporal-spatial gnosia and language functions.

The first patient had had drainage of an abscess of the frontal lobe and was left with residual generalized grand mal and petit mal seizures and episodic aphasia. Three years later the corpus callosum was sectioned completely, with resulting continuation of the convulsions and no major impairment of the higher functions. One year later the anterior commissure was cut, with the same results.

In the second patient, a depressed woman, the genu and the anterior half of the body of the corpus callosum, the anterior commissure and the right limb of the fornix were sectioned; this was followed by bilateral leukotomy. The higher functions studied in her case likewise were not impaired.

The authors concluded that there exist interhemispheral neuronal pathways other than those present in the corpus callosum and the anterior commissure.

WHITELEY, Philadelphia.

THE PHYSIOLOGICAL BASIS OF CONCUSSION. A. EARL WALKER, JERRY J. KOLLROS and THEODORE J. CASE, J. Neurosurg. **1**:103 (March) 1944.

With the use of general anesthesia, concussion was produced in a large number of cats, dogs and monkeys by the impact of a weight falling against the fixed skull. Tetanic spasm, respiratory and circulatory changes, alterations in reflexes and electrical disturbances were used as criteria of the concussive state. Cerebral concussion gave rise to the following clinical manifestations: (1) tetanic phenomena, consisting of immediate generalized muscular spasm, due to intense stimulation of the central nervous system; (2) respiratory changes, manifested by sudden spasm of the intercostal and diaphragmatic muscles, which produces a gasp, followed by normal or irregular respiration or by apnea; (3) changes in blood pressure, causing arterial hypertension, due to stimulation of the vasomotor centers, with production of peripheral vasoconstriction; (4) bradycardia, due to excitation of the vagus fibers, and (5) reflex changes, shown by the abolition of tendon reflexes and heightening of the threshold of the anterior horn cells.

The electroencephalogram revealed a generalized initial discharge, followed by a pronounced increase in the frequency of cortical activity, with subsequent relative inactivity and a gradual return to normal. The intense electrical discharge was conveyed to all parts of the nervous system.

The authors conclude that the physiologic basis of concussion is the traumatic breaking down of the polarized cell body membranes of the neurons of the central nervous system, with resulting firing of the axons, producing widespread excitation, both centrally and peripherally. The important factor in depolarization is the rapid oscillations in intracranial pressure. Furthermore, the altered permeability of the cell wall following breakdown of the membrane is the basis of postconcussion cerebral edema.

WHITELEY, Philadelphia.

PROBLEMS OF FATIGUE AS ILLUSTRATED BY EXPERIENCES IN THE DECOMPRESSION CHAMBER. JOHN ROMANO, GEORGE L. ENGEL, E. B. FERRIS JR., HENRY W. RYDER, JOSEPH P. WEBB and M. A. BLANKENHORN, War Med. **6**:102 (Aug.) 1944.

Forty-three adults were exposed repeatedly to simulated altitudes of 35,000 feet (10,250 meters) in a decompression chamber. They were studied clinically, psychologically and by various laboratory tests. In most cases each exposure was terminated because some incapacitating symptom of decompression sickness developed, but if none occurred the exposure was terminated at the end of three hours.

Three types of fatigue were observed: 1. Muscular fatigue occurred in all subjects, was unrelated to decompression sickness and disappeared with training. 2. Fatigue related to boredom occurred most often during exposures with no decompression sickness, when the subject remained inactive at the induced altitude for long periods. 3. The third type of fatigue was not related to muscular effort or to boredom. It was experienced by 24 of the 43 subjects and sometimes was related to decompression sickness and sometimes not. It was delayed in onset and resembled fatigue experienced during or after anxiety situations. The results of laboratory tests, including the electroencephalogram, the blood count and circulatory reactions to changes in posture, showed no direct correlation with any type of fatigue. In a few instances damage to tissues subsequent to decompression sickness undoubtedly contributed to the fatigue.

PEARSON, Philadelphia.

TONIC AND CLONIC RESPONSES OF THE CEREBRAL CORTEX FOLLOWING HYPERVENTILATION. EFREN C. DEL POZO, Arch. de neurol. y psiquiat. de Mexico **7**:35 (March-April) 1944.

The experiments recorded by del Pozo were performed on cats anesthetized with dial, the electrodes being applied directly to the cortex, which was covered only by the leptomeninges. The stimuli came from an induction coil at intervals of two or three minutes to avoid facilitation and extinction. Hyperventilation was produced by artificial respiration, with a cannula in the trachea. Blood pressure readings were taken by placing a cannula in the left carotid artery. The responses of the cortex to faradic stimulation were recorded electroencephalographically. In all cases hyperventilation caused diminution to disappearance of the usual cortical responses to faradic stimulation. In addition to shortening the duration of response, there was diminution of frequency and voltage of the electric potentials. The decrease in blood pressure during hyperventilation is not the cause of this diminution of cortical response. The author conducted experiments in which the fall

in blood pressure was avoided. The possibility of cortical inhibition due to an increase in afferent stimulation of the lungs and other viscera was ruled out by sectioning the vagus nerves and by performing experiments on animals with transverse sections through the midbrain. The same diminution of response during hyperventilation was observed. When artificial respiration was employed with air containing 4 per cent carbon dioxide, the cortical responses did not diminish or disappear. If the concentration of carbon dioxide was 8 to 10 per cent, the cortical responses persisted, even though no attempt was made to prevent lowering of blood pressure. The author offers no explanation of the mechanism for depression of cortical activity following faradic stimulation of the brain with hyperventilation. These results seem to contradict those of Brody and Dusser de Barenne, who reported an increase in responses to electrical stimulation of the cortex during hyperventilation.

SAVITSKY, New York.

PHYSIOLOGICAL INTERPRETATION OF THE CONVULSANT ACTION OF METRAZOL. CARLOS GUTIERREZ-NORIEGA, Rev. de neuro-psiquiat. **7**:14 (March) 1944.

Gutierrez-Noriega studied the action of metrazol administered in convulsant doses in decerebrate dogs. The experiments were performed on six groups of animals, transverse sections being made at various levels of the brain stem. Eight to 10 animals were used for each level, the sections being made (1) between the medulla and the pons, (2) at the midpons, (3) between the pons and the mesencephalon, (4) between the upper and the lower quadrigeminal tubercles, (5) above the mesencephalon and (6) above the hypothalamus. Metrazol was injected sixty to ninety minutes after operation; the dose (convulsant for normal dogs) was 20 mg. per kilogram for the first injection and 30 to 40 mg. per kilogram for the second injection, an hour later. The results of this experiment confirmed the observations of other investigators that the intensity and frequency of the convulsions diminish in direct proportion as the brain stem is cut at successively lower levels. It was further observed that tonic convulsions originated chiefly in the brain stem, specially in the medulla, pons and mesencephalon, while clonic convulsions had their origin in the upper nuclei (the mesencephalon, the hypothalamus and possibly the cortex).

Analysis of these results, together with the effects obtained by local injection and use of the Horsley-Clarke apparatus and bioelectric recordings, leads to the conclusion that the nerve discharges produced with stimulating drugs originate simultaneously or in rapid succession in many nerve centers. Summation, both temporal and spatial, takes place in the neurons of the spinal cord and the medulla and secondarily in other parts of the neuraxis, and the epileptic seizure follows. It is likely that the quantity of metrazol reaching each cell is subliminal for most of the neurons and that a liminal dose would be lethal. In all probability, the prolongation of the convulsion is due not to the continued action of the drug on the neurons but to the internuncial circuits of reexcitation.

The author calls attention to two theories regarding the pathogenesis of epileptic convulsions. According to one of them, the disturbance resides in the isolated neuron, the discharge rhythm of which is intensified or prolonged beyond the normal. The second theory admits no difference between the reaction of the normal neuron and that of the isolated neuron during a convulsion; the pathologic phenomenon resides in the entire neuron system and is due to the widespread summation and synchronization. The author's experiments tend to sustain the second theory, although the two are not in opposition.

PIETRI, New York.

SCHIZOPHRENIA AND PARANOID PSYCHOSES AMONG COLLEGE STUDENTS. THEOPHILE RAPHAEL and LEONARD E. HIMLER, Am. J. Psychiat. **100**:443 (Jan.) 1944.

Raphael and Himler studied the incidence and features of schizophrenic and paranoid psychoses in the student body at the University of Michigan. They found the incidence of schizophrenia to be 1 in 655 of the student population and that of paranoid disturbances to be 1 in 3,070. Schizophrenia was more common among male students and paranoid psychoses among female students. Forty-two per cent of the patients with schizophrenia were first seen in the acute phase of the illness. Students with paranoid psychoses were in the main considerably older than those with schizophrenia. Forty-four per cent of the patients were referred during their first semester. Evaluations of the personality at the time of admission to college showed a high incidence of unsatisfactory and doubtful ratings. Aided by regular contacts with the mental hygiene unit 46.1 per cent of the schizophrenic students and 60 per cent of the students with paranoid disorders were able to pursue their studies. The authors stress the importance of a proper screening of prospective students.

FORSTER, Philadelphia.

NEUROTIC REACTIONS IN PARACHUTISTS. JOSEPH G. KEPECS, Psychoanalyt. Quart. **13**:273, 1944.

All, or nearly all, parachutists fear jumping. This produces a conflict between the desire to escape and the demands of duty and personal pride. When a neurotic reaction develops, its occurrence and character depend on the sum of two factors: the man's life experiences, which, through the agency of repressed fears and unconscious fantasies, may invest a situation with terror far beyond the actualities, and the events of the traumatic situation, i. e., actual physical injury or narrow escapes.

Kepecs reports 5 cases of neuroses in parachutists and concludes that the neurotic symptoms express (1) attempts to repeat the traumatic situation, (2) efforts to escape the danger, (3) attempts to heal the wounds inflicted on the personality by the trauma, (4) attempts to repeat the trauma in terms of analogous threats to infantile existence which have been regressively reactivated and (5) other neurotic conflicts which parasitize on the available symptoms. The reactivation of infantile problems and the considerable degree to which the actual conflict is expressed in terms of childhood fears are attributable to three factors, which also shed light on the inability to give up the neurotic defenses after the way out of the danger has been successfully achieved:

1. A struggle against the social periphery of the superego, which is perceived also as a struggle against parental demands. This conflict has two phases: first, the attempt to escape the danger, and, second, the attempt to avoid recognizing the significance of the escape which the ego conceives as a defeat and which produces reproaches of cowardice from the superego. On a more immature level, this constitutes an escape

from dangerous activity by becoming passive, and it unconsciously signifies coming to terms with the father and escaping death by sacrificing the genital. The regressive expression serves as a defense against the recognition of the desire to escape.

2. The threat of destruction or dissolution of the personality overwhelms the ego and results in a contraction and diminution of the ego's powers. As a result the subject's adaptations take on an infantile character.

3. The direct threat to life and to the integrity of the body is connected symbolically and by association with specific early experiences, which may be regarded as sensitizing. Oral desires and oral ways of dealing with the world are important. Strong preexisting oral fixations appear to predispose to reactions of this type.

PEARSON, Philadelphia.

REMARKS ON THE COMMON PHOBIAS. OTTO FENICHEL, Psychoanalyt. Quart. **13**:313, 1944.

The simple phobic pattern is as follows: In a situation which unconsciously represents an instinctual temptation, anxiety is felt instead of excitement, and subsequently the situation, and therewith the anxiety, is avoided. The phobic situation does not always represent a sexual temptation, but may represent an aggressive impulse, an early frustration or an unconsciously feared punishment. If the anxiety is a warning signal against temptation, why does it become so severe? Anxiety functions as a danger signal to avoid the development of a traumatic situation when the organism is so flooded with emotion that the normal mechanisms for mastering excitation are inadequate. The function of anxiety fails in phobic anxiety. The ego, which gives the signal of danger, starts something which it cannot contest because the organism, through a series of previous repressions, has dammed up forces which are waiting the opportunity for discharge.

The temptation or punishment is displaced to the phobic situation as a ruse to escape greater dangers. In some cases an external object is substituted for another. In other cases there is an external projection of an inner danger, or a feeling of guilt is replaced by external fears.

All patients with phobias show regression the gains of which are secondary. Certain paths of displacement are determined directly by the specific nature of the warded-off instincts. For instance, a fear of being devoured serves the purpose of a defense against oral demands, of being on the street, against exhibitionism, and the like.

Agoraphobia wards off exhibitionism, scoptophilia and muscle pleasure in walking. There is a close connection between the sensory apparatus which registers anxiety and that which registers sensations of equilibrium and position in space. Conflicts emanating from the sexualization of infantile sensations of equilibrium give rise to equilibrial phobias. The sexualization occurs in some persons because sensation of equilibrium and of bodily movement in space has become the sole representation of infantile sexuality. In falling asleep and in anesthesia there occur equilibrial and spatial sensations. The association between these sensations and sleep leads to a phobia of death, and a high percentage of death phobias are phobias of sensation of equilibrium and of space. Fears of falling asleep and of being narcotized are expressions of underlying fears of being overwhelmed by psychologically painful sensations of disequilibrium in space.

Claustrophobia demonstrates the basic role of the projection of internal sensations. The patient dreads his own emotional excitement and attempts to escape from it by leaving the space in which he finds himself when the excitement occurs. The patient fears that his ego control will break down if he becomes enormously excited. The development of the clinical picture of claustrophobia is facilitated by two physiologic circumstances. First, the imposition of any hindrance to bodily movements, either real or fantasied, itself causes anxiety, through the damming of drives. Second, any state of anxiety is accompanied physiologically by a feeling of being closed in, so that an external closeness, or the idea of it, facilitates the mobilization of the entire anxiety syndrome.

The first physiologic syndrome of fear is a feeling of constriction in the chest, accompanied by difficulty in breathing. It is in an attempt to protect himself against unpleasant sensations that the patient with agoraphobia feels the street, and not his own body, as constricted or not constricted.

In some patients the underlying mechanism is that of projection. The danger instinct is projected, for example, onto the street, and then the patient is able to avoid the anxiety by avoiding the street. In other patients this does not happen, but the danger instinct constantly reemerges from repression and has to be projected again and again. This depends on the economic equilibrium between instinct and anxiety which results from the personal experience.

The person who requires stimulation or distraction to enable him to work well is really suffering from disturbances of concentration produced by an inner restlessness, which is relieved in surroundings which provide external restlessness, just as certain people may enjoy thunderstorms because, the noise being outside rather than inside themselves, they do not need to feel afraid of their own inner confusion and anxiety. There are innumerable prejudices and anxieties associated with types of landscapes, changes of weather and season, light and darkness, times of the day, and the like, which are narcissistic projections of inner feelings, for consciousness of nature is less a process of becoming aware of its physical elements than one of becoming aware of feelings evoked by the contemplation of these elements, or of the inner ideas which these elements symbolize.

The fear of overwhelming inner excitement is an important source of anxiety in the phobias. The fear of castration and the fear of being abandoned in childhood are the root of the fear that the ego will be flooded with unmanageable quantities of excitement because the child is not able to satisfy its demands. When the ego has developed sufficiently to achieve adequate instinctual satisfaction and to master reality, instinctual temptations should not be avoided as dangerous but should be anticipated as pleasurable. In the adult ego the idea that excitement is dangerous emerges only when satisfaction is frustrated by endogenous obstacles, i. e., by fear of castration or of loss of love, originating in an animistic misinterpretation of the external world.

PEARSON, Philadelphia.

STUDIES IN VITAMIN B DEFICIENCY WITH SPECIAL REFERENCE TO MENTAL AND ORAL MANIFESTATONS. A. GREY CLARKE and F. PRESCOTT, Brit. M. J. **2**:503 (Oct. 23) 1943.

Clarke and Prescott report the results of a study of 17 patients with deficiency of members of the vitamin B complex, which represented 2 per cent of all patients seen by them in an outpatient department. The nervous

disorders of all but 1 patient were classified as functional. The occurrence of oral lesions due to nicotinic acid deficiency associated with symptoms usually considered as psychoneurotic was a constant finding. All but 2 patients responded to therapy with members of the vitamin B complex. Three patients had relapses after periods of from two to five months without treatment but responded to further treatment. The study revealed a parallelism between the manifestations of a deficiency of the vitamin B complex and those of psychoneurosis.

ECHOLS, New Orleans.

PROGRESSIVE CEREBRAL ISCHAEMIA. TREVOR H. HOWELL, Brit. M. J. **2**:746 (Dec. 11) 1943.

Howell made a study of 27 senile patients, among whom were two groups whose mental deterioration seemed to be associated with cerebral ischemia. The first change noted was a vague or muddled state of mind in a patient previously lucid. This was followed by a stage of restlessness, often increasing to violence. As the restlessness wore off, the pulse became perceptibly weaker, and the patient drifted into a terminal coma. A progressive fall in blood pressure was noted in all cases in which readings were taken. Howell believes that the relation between a falling blood pressure and the appearance of cerebral symptoms in arteriosclerotic subjects suggests that progressive cerebral ischemia is the basic pathologic condition.

ECHOLS, New Orleans.

NERVOUS BREAKDOWN IN THE NAVY: DOMESTIC DIFFICULTIES AS A CAUSAL FACTOR. GEOFFREY TOOTH, Brit. M. J. **1**:358 (March 11) 1944.

Of the environmental factors which cause nervous breakdowns in the Navy, the two which are not directly connected with hazards of war are (1) the conditions and the type of service and (2) domestic difficulties. Tooth studied the effects of these factors on patients in two hospitals in different parts of the world. It was noted that 35.6 per cent of the men with nervous breakdowns due to domestic difficulties were invalided, whereas 26.6 per cent had breakdowns leading to invalidism because of enemy action or conditions of service. It was further observed that when there are multiple etiologic factors of which one is domestic trouble, the virulence of the reaction was twice as great as when domestic worries alone were responsible. Analysis of the types of domestic difficulties revealed that the most frequent cause of breakdown was real or suspected infidelity of the wife or fiancée, with illness or death of a near relative a close second. The author emphasizes the need for thorough investigation of cases and suggests that a psychiatric social worker be appointed to Naval depots in an effort to reduce the incidence of nervous breakdowns leading to invaliding as a result of domestic worries.

ECHOLS, New Orleans.

ANXIETY; ALOPECIA AREATA; NEUROFIBROMATOSIS; AURICULAR FIBRILLATION. DOUGLAS HUBBLE and C. H. ROGERSON, Brit. M. J. **1**:486 (April 8) 1944.

Hubble and Rogerson report an unusual case of a patient exhibiting three disorders of unknown cause and pathogenesis: alopecia areata, neurofibromatosis and auricular fibrillation, each of which developed at the peak of a period of great frustration and anxiety. The patient, an intelligent, impulsive, resentful person, possessed exceptional drive and ambition, with an obsessional desire for success. The authors postulate that in this case the auricular fibrillation and the alopecia areata were related to the neurofibromatosis. Quinidine therapy resulted in resumption of normal cardiac rhythm. The case represents the varied factors (genetic, constitutional, psychologic, environmental and mechanistic) which must be taken into consideration when one is evaluating disease in man.

ECHOLS, New Orleans.

THE RELATION OF DERMATOLOGY TO PSYCHIATRY. F. F. HELLIER, Brit. M. J. **1**:583 (April 29) 1944.

Hellier discusses the significance of the psychologic approach in the study of dermatologic conditions, for "embryologically speaking at least, psychiatry is an offspring of dermatology, and a fundamental association persists into adult life." Of the two groups of cutaneous conditions (cutaneous diseases proper and cutaneous reactions) the latter is primarily concerned with the makeup of the patient. Consequently, treatment should be based on the discovery of the immediate factor which caused the present attack and the adjustment of the patient's attitude to life and his dermatologic condition. The latter may be difficult to accomplish, but it is most important if permanent benefit is to be obtained. Among the cutaneous reaction diseases discussed are eczema, rosacea, alopecia areata, lichen planus and hyperhidrosis.

ECHOLS, New Orleans.

CARDIAC NEUROSIS [NEUROCIRCULATORY ASTHENIA] AS A MANIFESTATION OF HYPOGLYCEMIA. R. GREENE, Lancet **2**:307 (Sept. 2) 1944.

Greene describes 5 cases in which the clinical symptoms were interpreted as those of DaCosta's syndrome (effort syndrome), or neurocirculatory asthenia. In all cases there were precordial pain, giddiness or faintness and perspiration on exertion of mild to moderate degree. In some cases headache, palpitation or tachycardia was present as well. In each case there was laboratory evidence of hypoglycemia when the attacks were reproduced. All attacks were aborted by administration of sugar. Each patient had a normal heart.

Since neurocirculatory asthenia is brought on by fear, which, in turn, causes liberation of epinephrine, and since the early symptoms of hypoglycemia are those of epinephrine activity, it is not surprising that the two conditions may be confused. Indeed, they "are identical." Since the symptoms of hypoglycemia may be relieved by adequate diet, "an effort should be made to evaluate the part played by abnormal carbohydrate metabolism in producing the symptoms of each patient with DaCosta's syndrome or a similar cardiac neurosis."

MCCARTER, Boston.

Meninges and Blood Vessels

GLYCOSURIA IN MENINGITIS. FRANK FERGUSON and DAVID BARR, Ann. Int. Med. **21**:173 (Aug.) 1944.

Ferguson and Barr report their observations on 72 consecutive patients with meningitis. Spontaneous glycosuria occurred in 16 of the patients and in over one third of the 26 patients who had meningococcic meningitis. Glycosuria was encountered in cases of meningitis caused by the meningococcus, pneumococcus, staphylococcus and tubercle bacillus. In 1 patient the organism was not isolated. Ketosis, hyperglycemia and diminished dextrose tolerance frequently accompanied

the glycosuria. The glycosuria was transient, and it persisted beyond the third day in only 3 of the 16 patients. Coma with glycosuria and ketosis at the onset of meningitis may lead to a faulty diagnosis of diabetic ketosis. Delay in the establishment of a correct diagnosis of meningitis and subsequent proper management may have serious consequences.

GUTTMAN, Philadelphia.

MENINGOCOCCIC MENINGITIS: SULFADIAZINE THERAPY. EMIL H. GRIECO and ARTHUR M. COVE, Ann. Int. Med. **21**:194 (Aug.) 1944.

Grieco and Cove report clinical and laboratory observations on 20 consecutive patients with meningococcic meningitis. As soon as the diagnosis was established, an initial dose of 5 Gm. of sodium sulfadiazine was administered intravenously, even when the patient could take the drug orally. Subsequent doses of 2 Gm. were given regularly every four hours, either orally or intravenously, as determined by the patient's ability to receive medication. One gram of sodium sulfadiazine was administered every four hours until the temperature returned to normal, and from this point, four times a day daily for the next seven days. As long as the urinary output was 750 cc. or more during the first twenty-four hours fluids were not administered parenterally. This method of sulfadiazine therapy afforded adequate concentrations of the drug in the blood, effected satisfactory clinical response and resulted in few complications, none of which left permanent residua.

The Waterhouse-Friderichsen syndrome was encountered in 2 patients, 1 of whom recovered after the parenteral administration of an aqueous extract of adrenal cortex.

GUTTMAN, Philadelphia.

MENINGOCOCCEMIA WITHOUT MENINGITIS: A STUDY MADE AT THE STATION HOSPITAL, FORT GEORGE G. MEADE, MARYLAND. HAROLD W. POTTER, ROGER D. REID and LEWIS H. BRONSTEIN, Ann. Int. Med. **21**: 200 (Aug.) 1944.

Potter, Reid and Bronstein report clinical observations on 11 patients who had meningococcemia without evidence of meningitis. The outstanding and most useful sign was the cutaneous eruption. Only 1 of the 11 patients failed to exhibit this sign. Joint and muscle pains, present in 6 of the 11 patients, formed another outstanding characteristic of the syndrome. Headaches were present in 10 of the 11 patients.

The authors conclude that "the diagnosis can be strongly suspected before the report of the blood culture in a patient with the skin eruption and headache if the possibility of this disease is kept in mind. Sulfadiazine resulted in rapid cure without sequelae in all our cases."

GUTTMAN, Philadelphia.

FULMINATING MENINGOCOCCIC INFECTION (WATERHOUSE-FRIDERICHSEN SYNDROME). P. A. HERBUT and W. E. MANGES, Arch. Path. **36**:413 (Oct.) 1943.

Herbut and Manges review the history of the Waterhouse-Friderichsen syndrome and report 4 cases, which bring the total number to 125. Because of the rapid onset and the high fever, often associated with leukocytosis and a fulminating course with fatal termination, the syndrome has long been regarded as an overwhelming septicemia. Although the meningococcus has been shown to be the causative agent in over 60 per cent, the authors believe that this figure is much too low. It is the consensus that adrenal apoplexy is responsible for the death of the patients. The authors, however, concur with Aegerter that there is no proof that death from the Waterhouse-Friderichsen syndrome is due to adrenal failure rather than to toxicity caused by invasion of the blood stream. In 3 of their cases there were bilateral and massive adrenal hemorrhages. In the fourth case only a single small, circumscribed hemorrhage was noted in the right adrenal gland, while the medulla of both glands showed areas of hypoplasia. Sections of skin in 3 cases showed, respectively, congestion of the dermal capillaries; congestion, hemorrhages and inflammation, and congestion, hemorrhages, inflammation and thrombosis. In 3 cases with predominantly septicemic symptoms there were dissociation of the hepatic cords, cloudy swelling of liver cells, sinusoidal congestion, perisinusoidal edema and diffuse infiltration with polymorphonuclear leukocytes. Meningococci were isolated post mortem in pure culture from the spinal fluid and the blood from the heart in 1 case and ante mortem from the spinal fluid and material from the nasopharynx in 1 case. Cultures of the blood taken post mortem in the remaining 2 cases yielded respectively a member of the Friedländer group and Staphylococcus aureus. Sections of the skin in each of these cases and of the adrenal gland in the former cases disclosed within the capillaries gram-negative, bean-shaped diplococci, morphologically similar to meningococci. It is probable, therefore, that in most, if not all, of the cases of the Waterhouse-Friderichsen syndrome in which other organisms have been isolated the disease was caused by meningococci.

J. A. M. A.

MENINGITIS DUE TO PITTMAN AND NON-PITTMAN STRAINS OF H. INFLUENZAE. J. GORDON, H. E. DE C. WOODCOCK and K. ZINNEMANN, Brit. M. J. **1**:779 (June 10) 1944.

Gordon, Woodcock and Zinnemann report 2 cases of meningitis due to the non-Pittman type of Haemophilus influenzae in which treatment with sulfapyridine was successful. The strains of H. influenzae isolated in these cases did not differ from the strains regularly isolated in cases of bronchiectasis. Because so few cases of meningitis due to H. influenzae typed serologically have been reported, the authors describe 3 cases in which the strains isolated were of Pittman type B; in 2 of these 3 cases in which the course was fulminant and fatal, little or no treatment was given. In the third case response to sulfapyridine treatment was good, but more of the drug was required than in the 2 cases of meningitis produced by the non-Pittman type. Because so little is known of the relative response of non-type-specific and type-specific strains of H. influenzae to the sulfonamide compounds, the authors believe that in cases of meningitis of this origin, the organism should be typed, in an effort to determine any possible differences in prognosis.

ECHOLS, New Orleans.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

PAUL I. YAKOVLEV, M.D., *Presiding*

Regular Meeting, March 16, 1944

Psychiatric Problems in Conservative Treatment of Ulcerative Colitis. DR. ERICH LINDEMANN.

For 45 patients with ulcerative colitis, verified by proctoscopic examination, the psychosocial history, the personality makeup and the response to therapeutic interviews were studied. The history showed various forms of bereavement as the most important precipitating factor. For 26 of the 45 patients a close time relation existed between the loss of an important person and the onset of the illness. Ten other patients had ceased to interact with an important person because of disillusionment or rejection. A surgical procedure preceded the onset of the illness of 4 patients. Three patients had shown notable behavior abnormalities, and the onset of the illness was preceded by signs of a beginning psychosis, which, however, did not develop further after the colitis started. The personality of the patient was marked by poverty of human relationships, an inability to make and hold friends of their own age, and by a need for considerable activity throughout the day but lack of resourcefulness in finding avenues for such activity. Rewarding patterns of social interaction seemed not to be indigenous to these patients. This state of affairs became conspicuous only when a key person on whom the patient was dependent and from whom he had borrowed patterns of interaction was removed from the "social field." This dependency, which seems to be a special form of social integration, became a threat to the patient after bereavement because he was then confronted with a poverty of successful patterns of conduct and with a tendency to primitive behavior patterns, colored by fantasies of extreme violence and social behavior marked by aggressiveness and overcritical, demanding and "spoiled-child" attitudes. This trait was often shown in the request for consultation from the medical service.

Such inclination to primitivation of behavior (regressive tendencies?) often becomes manifest only after the psychiatrist has established growing intimacy with the patient in interviews. Early attempts at exploration with the usual psychiatric technic of reconstructing the life history were invariably followed by a primitivation of the patient's fantasies and behavior. The patient would leave treatment, not to return until vigorously urged by the internist, or would develop overwhelming anxiety from fear of being overcome by primitive impulses or would report actually having experienced psychotic manifestations, such as auditory hallucinations, a sense of alien influence or somatic delusions. Other patients became conspicuous in the ward through dilapidated behavior, such as impulsive outbursts or defecating on the floor, and needed special nursing care. The behavior, stream of talk and communicativeness in explorative interviews rapidly changed to uncommunicativeness, retardation and often blocking. Objective time records of the verbal and gestural activity during interviews (interaction chronogram) demonstrated a remarkable reduction in the capacity for interaction during progressive interviews.

It became evident that the patients were as vulnerable to the establishment of new contacts as they were to the loss of social interaction.

The reactions shown by the patient were strikingly similar to behavior patterns associated with acute grief, which were studied after the Cocoanut Grove disaster.

The technic of psychologic management must avoid the traditional methods of psychoanalytic inquiry. The contact must be brief, not permitting the development of regressive tendencies, hostile feelings or affectionate attachment. The relationship must, rather, be an identifying one, in which the patient copies behavior patterns of the psychiatrist and makes use of them in the same manner as he previously did with the patterns of the person whom he has lost. If this difficult problem is solved, the patient usually goes through a period of imitating the psychiatrist in his relations with other patients in the ward, and of idealizing the psychiatrist, attributing to him an inordinate status in the hospital and testing out his availability and willingness to serve the patient as a source of new patterns of conduct. After such a relationship is established, it is often possible to review the bereavement with the proper emotions of depression and sorrow. The patient may go through a period of "nervousness" and worry, which might, superficially, appear detrimental to visceral functions but which is a prerequisite for readjustment.

While the personality, the precipitating crisis and the habitual reaction patterns of the patients seemed uniform, ulcerative colitis did not develop in the large majority unless another, somatic, factor brought about a special predisposition in the colon. Gastrointestinal disturbances in the family, acute gastrointestinal infections, measles with gastrointestinal involvement and surgical procedures seemed to be nosogenic. Psychologic determination in terms of traumatic experiences in childhood was rare; in only 2 patients did I find a confirmed history of severe difficulties in bowel training. In no patient did mucous colitis precede the ulcerative colitis.

DISCUSSION

DR. STANLEY COBB: I should like to emphasize first the fact that the psychiatrist is working with the physician, and working on equal terms. It used to be a matter of handing the patient over completely, not working on an equal footing. Patients used to be handed back and forth, again and again. Here, at last, the internist and the psychiatrist have worked out a method of working together.

Second, Dr. Lindemann has introduced something new in psychiatric therapy. It has been taught for years that the method of chief reliance was exploration through interviews. This exploration was efficacious in many cases. In cases of ulcerative colitis it is harmful.

Last, Dr. Lindemann is to be congratulated on working with an anthropologist. With Dr. Chapple's invention of actually measuring certain interpersonal reactions, one does not have to rely on impressions after an interview. All this leads in the right direction. Psychiatric interviews can eventually be made something worthy of the name of science.

DR. CHESTER M. JONES: The significant feature of Dr. Lindemann's presentation is the clear demonstration of the importance played by emotional disturbances in a chronic organic disease involving the digestive tract, such as chronic ulcerative colitis. In this disease, psychiatric considerations comprise only one of several significant factors; but because the underlying cause of the disease is still not known, it is of extreme importance that each of the various factors be controlled as completely as possible.

There can be no doubt that adequate psychiatric measures are helpful in controlling the activity of ulcerative colitis in numerous instances. At times psychotherapy may constitute a real hazard to the patient's health because of resulting emotional disturbances, transient though they may be. For this reason it is important that the psychiatrist and the internist collaborate closely, shifting responsibility as the need arises, so that the patient as a whole may be adequately observed and controlled as nearly as possible.

The importance of overstimulation of the autonomic nervous system secondary to emotional disturbances cannot be overemphasized and probably represents a fundamental conception of gastrointestinal physiology which involves not only this disease but many other conditions, such as ulcer and diverticulitis. Symptoms referable to the digestive tract probably represent nothing more or less than an exaggeration of the normal physiologic processes involving motility, local or general blood supply, tonus and secretion. All these factors may be conditioned by disturbances involving the autonomic nervous system. These changes have been clearly demonstrated by Wolff in his work on the stomach and by White and Jones in their observations on the sigmoid portion of the colon.

DR. H. HALE POWERS, Wellesley, Mass.: While Dr. Lindemann was speaking, I was reminded of a case that occurred in my experience almost thirty years ago. The young woman had previously been treated for ulcers of the colon in one or two hospitals; then she recovered under treatment with bromides and only a little psychotherapy. I do not know how long she remained well.

I have been wondering how patients with ulcerative colitis differ in personality from patients with gastric ulcer. Patients with gastric ulcer whom I have known have been as socially inclined as the average. As Dr. Lindemann has said, it is perhaps well for physicians to react, to a limited extent, against psychoanalysis. The goal is to keep patients as normal as possible, and the normal person has a certain content in his mind that he does not disclose to any one. Psychologic exploration should not be carried out unnecessarily, any more than surgical exploration. Surgical exploration can produce adhesions. One knows many patients who are adherent to certain psychiatrists. In those patients psychologic adhesions have been produced.

DR. FRANK C. D'ELSEAUX: Dr. Lindemann and Dr. Jones have demonstrated that an internist and a psychiatrist can, and in cases of ulcerative colitis must, work in close association with each other. Dr. Jones has pointed out that in many cases the disease starts with an intestinal infection which may be common to a number of people, in only 1 of whom ulcerative colitis will develop, and that the large bowel shows circulatory changes under emotional strain. I wonder whether it may be said that the patient who subsequently has ulcerative colitis uses his bowel in a different way psychophysiologically throughout life and that his bowel is, therefore, more vulnerable to infection, and subsequently to ulceration.

Dr. Lindemann stressed the important function of "role psychiatry." While such a method has been used by many psychiatrists, it is doubtful that any have used it so wholeheartedly as has Dr. Lindemann, with such careful attention to detail or with such full realization that unless it is carried out in such a manner it may do more harm than good, harm which may be fatal to the patient with ulcerative colitis.

I wish that Dr. Lindemann, who obviously has much greater knowledge of the psychologic mechanisms involved than he indicated in his paper, had not limited himself to pointing out a mere temporal relation between occurrence of a qualitatively specific incident and the appearance of a symptom in a patient with certain personality attributes. I wish he had given more dynamic insight into why this type of personality develops, why the patient has come to have this special dependence and restriction of objects on which he is dependent, and why when there are so many leave-takings, he reacts more strongly than others to separation. One wonders what is the special meaning of a separation to such a person. One also wonders why the bowel is the origin of election and why ulcerative, instead of mucous, colitis develops.

Finally, I should like to ask Dr. Lindemann how he feels about the use of a more deeply investigative type of therapy during a period of remission, or whether this must be modified even then.

DR. J. MARTIN WOODALL: Many of the patients with colitis seem to do extremely well symptomatically with a nonexploratory type of therapy. I can speak particularly of patients with mucous colitis, with whom I have had an extensive experience. Psychiatrists who deal with the psychoneuroses in an organized hospital setting, where an opportunity is afforded for detailed observation, have frequently noted the extraordinary influence on the patient's symptoms of his reaction to other persons—to the physician, to a nurse or to another patient. This is particularly noticeable with symptoms of a psychosomatic nature. Such an interpersonal relationship can be a potent factor in the control of symptoms seriously interfering with normal physiologic processes. The delineation of the components of such a relationship gives invaluable information as to the dynamic basis of the patient's illness and furnishes important clues to the methods to be employed in appropriate general management. If subsequent exploratory therapy is indicated, this interpersonal reaction becomes the foundation for its organization. Dr. Lindemann is to be congratulated on so lucid and comprehensive a presentation of an extremely informative paper.

DR. G. COLKET CANER: I should like to ask Dr. Lindemann whether any particular type of emotion brought on exacerbations of this condition.

DR. PAUL I. YAKOVLEV: I wish to ask Dr. Lindemann to what extent these emotional situations to which the patient is responsive are of his own making. Are the situations a projection of the personality of the patient, or are they a part of his own background?

DR. ERICH LINDEMANN: I wish to thank the discussers, especially Dr. Jones, who has been helpful in giving a proper balance to the discussion. What I said would have been one sided if he had not emphasized the internist's point of view. In this work I found it extremely interesting to treat a condition in which a severe structural disorder had to be approached by psychiatric methods. New skills had to be developed. These methods are related to what Whitehorn used to call supportive therapy of the psychoses. They are similar

to methods used with children, especially young children, and allow a limited expression of primitive behavior. These ideas are not as new as they seem.

In answer to Dr. Powers and Dr. D'Elseaux, I must have given the false impression that I was proposing to give up exploration altogether. This is not true. Exploration is impossible only for the emergency state of ulcerative colitis; similarly, I should not recommend it for schizophrenia. Certainly, after the emergency period which I stressed is over, the patient enters another phase of the illness, in which one learns a good deal by exploration about the patient's former development and about his present defective social relationships. In the latter the patient will recapitulate his childhood habits of behavior. One of the most fascinating problems which arise is this: In what way has it come about that such a person has not learned to acquire more lasting relationships? Why has he not acquired lasting patterns of effective behavior? Why can some of them behave effectively only when a certain key person is present? Sometimes the answer is to be found in the patient's early background. For instance, a boy whose father's patterns of behavior are objectionable to him may copy his mother as a model and become a "sissy." His subsequent social isolation comes from wrong steps in the early acquisition of patterns of social interaction. Evaluation of the early influences in the patient's life is important, but one must not mobilize dangerously powerful emotions connected with some early experience. A good deal of information may be gained, however, not from exploration but from observation of the patient's interaction with other patients. For instance, the young girl whose case I discussed had a delayed grief reaction to the death of her mother following an abortion, which occurred when she was 3 years old; this reaction was acted out in the ward but was not recalled as a memory. Two weeks after I started psychiatric work with her, she had a panic attack in the middle of the night. The house officer was called. The patient showed him a bit of stool which she believed to be an embryo. Identifying herself with her mother, she wondered whether she was aborting and whether she must die too. The next week she refused to eat, being afraid of finding drugs in her food such as her mother used to induce an abortion. A week later she was in a severe depression, with feelings of self depreciation. She was blaming herself for seeming to try to separate her father and stepmother. In all this, exploration in verbal terms was replaced with observation. The situation is much like that encountered in child psychiatry; I use observation of behavior, much as is done in the play technic.

Dr. Woodall, I agree that patients with psychosomatic disturbances as a group are so dangerously ill that supportive treatment is important. With respect to the organ of choice, patients with ulcerative colitis and patients with peptic ulcer present quite different problems. There is much similarity between patients with rheumatoid arthritis and patients with ulcerative colitis. Ten per cent of patients with ulcerative colitis have rheumatoid arthritis.

In reply to Dr. Caner's question, I am cautious in using the term emotion because it is so vague. The essential emotion in cases of ulcerative colitis is sorrow. My work with patients with this disease was what started me working on grief reactions, and I have found that these patients present an abundantly interesting area for psychiatric study and treatment.

HARRY C. SOLOMON, M.D., *Presiding*

Regular Meeting, April 20, 1944

The April meeting of the society was held at the Boston Psychopathic Hospital for the presentation of clinical material by the members of the hospital staff. The latter reviewed briefly some of the problems which are of interest to the members of the staff or which might intrigue the members of the society or which offered some novelty.

The program consisted of rapid presentations of the effect of frontal lobotomy and a modification of the surgical technic of this procedure; a preliminary review of the effect of penicillin on neurosyphilis; a consideration of the possible damage to the mentality of patients who have received electric convulsion therapy, and the use of sodium amytal in the exploration of the psychic content of an apprehensive or inhibited patient.

Frontal Lobotomy. DR. JAMES L. POPPEN.

The experience which my associates and I have had with frontal lobotomy has been so recent that as yet we are not justified in expressing a dogmatic opinion as to the proper method of carrying out the leukotomy. It is through the efforts of Dr. H. C. Solomon that Dr. Horrax and I have been urged to attempt relief of the dreadful anxiety which some of the patients suffer.

Several methods have been advocated for carrying out an adequate leukotomy. Watts and Freeman deserve considerable credit for corroborating the work of Egas Moniz and for popularizing the procedure. Since the technic of Lyerly seems to be a more adequate surgical approach, I have adopted his plan, with a few minor modifications. Two trephine openings are made 2.5 cm. in diameter. A button of bone is removed from each side of the skull 3.5 cm. from the midline just anterior to the coronal suture line. A small dural flap is made. A ventricular needle is then inserted into the most anterior portion of the lateral ventricle. As it enters the ventricle, it is withdrawn, directed just in front of the anterior pole of the lateral ventricle and inserted until the ridge of the sphenoid wing is felt. The needle is then withdrawn, and the tract acts as an excellent guide to the direction and plane of the incision in the white matter that is to be made by the electrosurgical suction unit. A lighted retractor gives excellent exposure and visualization, allowing the surgeon to perform a complete leukotomy and, at the same time, to save all the larger branches of the cortical vessels as they are encountered medially, inferiorly and laterally. The anterior cerebral artery can be well visualized and therefore protected from injury. The falx can be seen through the arachnoid, with the larger cortical vessels left intact. It is important that the white substance just anterior to and beneath the lateral ventricle be completely divided down to the ridge of the sphenoid wing. In our first case the symptoms recurred a few days after operation. The incisions were reopened, and it was noted that the white matter between the anterior horn of the lateral ventricle and the ridge of the sphenoid wing had been incompletely sectioned. Notable improvement in the patient's condition occurred after the dissection had been completed.

No changes in the state of consciousness have been noted in the patients operated on after they aroused from the anesthesia.

The operation, though seemingly minor, should not be undertaken lightly. All the more conservative measures

should be given adequate trial for a sufficient period. Unfortunately, in this particular operation the neurosurgeon is, and should be, merely a technician. The decision as to the suitability of the patient for operation falls directly on the shoulders of the well trained psychiatrist. The operation is safe only in the hands of a competent neurosurgeon.

CHICAGO NEUROLOGICAL SOCIETY

R. P. MACKAY, M.D., *President, in the Chair*

Regular Meeting, April 11, 1944

The Future of Neurology: Presidential Address. DR. R. P. MACKAY.

Erotomania (Lymphomania) as an Expression of Cortical Epileptiform Discharge. DR. T. C. ERICKSON, Madison, Wis.

This paper was published in full in the March 1945 issue of the ARCHIVES, page 226.

Effects of Lesions of the Periaqueductal Gray Matter in Cats and Monkeys. DR. PERCIVAL BAILEY and DR. E. W. DAVIS.

Patients with lesions around the midbrain sometimes pass into a strange state, which has been called "akinetic mutism." It was thought possible that the periaqueductal gray matter, a very old and fundamental formation in the brain stem, might be related to this condition. After some experimentation, a method was developed of destroying this nerve tissue without injury to other parts of the brain. The effect on cats was to reduce their activity almost to zero when the lesion was extensive. An aggressive, dangerous male monkey would sit apathetically in a corner of the cage. If he was given food, he would eat but would not bother to move for it if it was out of his reach. If he was irritated roughly, he would bare his teeth but make no attempt to attack. In general, the behavior of all these animals was characterized by this lack of "drive." Serial sections through the brain proved that the injury had been confined to the periaqueductal gray matter in almost all cases. Extension of the lesion into the periventricular gray matter of the diencephalon added a cataleptic component to the syndrome. The animals were not unaware of their surroundings but reacted much less actively and less continuously to their environment and lapsed quickly into indifference. (The behavior of the cats was illustrated by motion pictures, and photographs of the lesions were demonstrated.)

It is tempting to correlate these observations with dynamic psychology. These basal formations are obviously closely related to the instinctive drives and are regulated and controlled by the vast superstructure of the cerebral hemispheres. In man, however, one must remember the steady corticalization of many functions subserved in lower vertebrates, even in lower mammals, by subcortical mechanisms.

DISCUSSION

DR. R. P. MACKAY: One is reminded of Dr. H. Douglas Singer's theory that lesions of the diencephalon underlie schizophrenia. The behavior of certain of these akinetic animals does suggest catatonic stupor. Perhaps this interesting work may lead to something important in the field of this disease.

DR. VICTOR E. GONDA: May I ask for a somewhat more detailed description of the technic with which the authors could so exactly induce such a well circumscribed lesion with electric current?

DR. PERCIVAL BAILEY: The lesion was made with an electrical apparatus which delivers a constant amperage. The behavior we have described was first observed by Magendie. He produced it in unanesthetized rabbits by destruction of the heads of both caudate nuclei. Mettler obtained it with removal of the frontal lobes. I have seen Mettler's moving pictures of his animals. The ability to progress in our animals is better than in his; his animals showed leaping rather than progression. Dr. Davis and I tried to reproduce this behavior by removal of the frontal lobes, but were never able to get results as good as Dr. Mettler's. Just what the mechanism is that releases such behavior I do not know.

Book Reviews

Foster Home Care for Mental Patients. By Hester B. Crutcher, Director of Social Work, State of New York Department of Mental Hygiene. Price, $2. Pp. 199. New York: The Commonwealth Fund, 1944.

This book deals with foster home care for mentally ill patients. The author discusses the meaning and values of family care, including administration and the results achieved, the selection of patients, the selection of homes and the supervision of the patients, giving case histories to illustrate her observation. Miss Crutcher describes two methods of organizing family care: the colony and the district system. Family care of the mentally ill has existed for some time, both in this country and in some other countries, but it has not been an adequately developed or adequately staffed community procedure in the United States.

For a long time state hospitals in this country have needed relief from overcrowding. Family care is a good means of meeting this problem. Even with wartime difficulties there are in the state of New York at present as many patients under family care as would almost fill a state hospital. In this state only patients who are unable to work for their own maintenance or to look after themselves if given a relief check are classified as family care patients. The program began in 1933, with the placement of mentally defective patients. It was first financed by colony funds, which had accumulated over a period of years.

Thirty-two women patients, who had been in one institution many years, were placed in homes which were considered ideal for care of patients of this type. The women adjusted so well that the number was increased as rapidly as funds for such care were available. So successful was this placement of mentally defective patients that in 1935 legislative authorization was provided for the family care of the mentally ill. Each institution was allowed to use maintenance funds for the placement of patients under family care with the understanding that a deficit up to $10,000 in this sum would be allowed by state budgetary authorities. This placement plan of the mentally ill has been developing slowly and carefully. In general the institutions developing the program have placed patients in homes within a 30 mile (48.3 kilometer) radius of the institution. However, both Letchworth Village and Middletown State Hospital have placed patients in a rural area about 75 miles (120.6 kilometers) from both institutions. This area of the state was regarded as ideal for the extensive development of a family care program, especially for the patient requiring continuous treatment. After three years there were over 600 such patients living with families in various parts of the state. It was felt that a good foundation had been laid for the relatively rapid development of the program, when its financial support was withdrawn. Fortunately, permanent restoration of funds for continuing this work was made on July 1, 1940, so that, again, patients can enjoy the advantages of community life. The New York State Department of Mental Hygiene has been responsible for the allocation of funds and for the general direction of the program.

The rate paid by the state was originally $4 a week, but this has since been raised, and the present weekly rate ranges from $6 to $8, with an allowance of 25 cents a week to the patient for spending money. Clothing is furnished by the institution responsible for the patient if no relatives or friends can be found to furnish this. Patients who have funds of their own or whose relatives are willing and able to pay more than the state rate are placed in family care accommodations in keeping with the amount paid for the patient's care. Usually, 1 to 6 patients are placed in a home. However, in certain instances, spacious homes have been found which accommodate 10 to 15 mentally defective patients.

Seventeen of the twenty civil state hospitals and three of the five state schools have family care programs. At the beginning of the present war approximately 1,900 patients were under family care, but, owing to shortage of personnel and changes in family life, this number has gradually decreased. As of Jan. 1, 1944 approximately 1,800 patients were in family care, the ratio of patients receiving family care to patients in state hospitals being 1.5 per hundred, and the ratio of mentally defective patients receiving family care to those in state schools, 3.1 per hundred. The large state hospitals in New York city have not been able to develop family care to any great extent. One or two elderly patients are thus placed in some homes. When these patients have shown they can adjust and manage their financial affairs, they are transferred onto convalescent status with old age assistance. Patients suitable for family care are selected and transferred to hospitals in the upstate district where homes are available. In spite of the present shortage of medical and social service staff and the curtailment of transportation facilities, the service is now firmly established as a supplement to institutional care.

The book is recommended as describing and evaluating an important adjunct facility for the care and rehabilitation of the mentally ill.

Freud's Contribution to Psychiatry. By A. A. Brill, Ph.B., M.D. Price, $2.75. Pp. 245. New York: W. W. Norton & Company, Inc., 1944.

Brill was the Salmon lecturer in 1943. He chose to discuss Freud's contribution to psychiatry, and these lecturers are now available in book form. Brill is the translator of many of Freud's books and his close and faithful friend for many years.

Much of the volume is concerned with the history of the development of the psychoanalytic movement. The first three chapters concern Dr. Brill's introduction to psychoanalysis, from the descriptive psychiatry then in vogue in New York to the interpretive psychiatry in Europe. Brill's quest for knowledge concerning hypnotism led him to Paris, just as Freud had been led earlier. He then studied at Burghölzli, where, together with his chief, Bleuler, and Jung, Riklin, Abraham and Hans Meier, Freud's association technic was first used. A résumé of Freud's professional life follows this introduction. The whole development of psychoanalysis is unfolded, beginning with Freud's fascination by hypnotism, his studies of hysteria and his first attempt to describe a case psychoanalytically, namely, the famous

Dora case. By 1908 Freud's basic works had been written, and of these "The Interpretation of Dreams" was the most significant.

The remainder of the book is devoted to presentations of the most notable theories, ending with Freud's final preoccupation with man and race and the postulate that all disturbances in these spheres have their origin in the Oedipus complex. Brill stresses particularly Freud's belief that the psychoses differ from the neuroses in degree rather than in kind and that psychoneurotic illness never occurs in a person with a normal sexual life. Most of the concepts are illustrated by Brill by his own cases, which he interprets in a strictly freudian manner.

This book of 234 closely printed pages affords pleasant and informative reading. There are glimpses of the author's quiet humor, which add charm and at the same time make one sense his humility. The book constitutes an excellent summary of Freud's own vast psychoanalytic contribution, seen through the eyes of his American pioneer. Time alone will show the inherent value in all his theories. Psychoanalysis is slowly changing and growing, and a clear knowledge of its origins is essential to all who wish to interpret these changes, as well as to students of the problems of people and their relationships. The volume is highly recommended.

Insulin Shock Therapy Study. By the Temporary Commission on State Hospital Problems. Pp. 97. New York, 1944.

This study of the effectiveness of insulin shock in the treatment of schizophrenic patients is the report of the Temporary Commission on State Hospital Problems, appointed by Gov. Thomas E. Dewey of New York. The study is based on the results of insulin therapy of 1,128 patients at the Brooklyn State Hospital between January 1937 and June 1942, and the data for a control group of 876 patients admitted to five other state hospitals during the same period who did not receive any form of shock therapy but whose treatment was presumably comparable in other respects. The most dramatic finding emerging from this study is that insulin treatment effected a saving of 286,695 days of hospital care and a saving of $80,274.60 in cost of food and clothing to the state. Accepting the validity of the non-insulin-treated patients as a control group, the commission concludes that the insulin treatment itself was the significant differential factor in reducing the period of hospitalization. The natural recommendation is made that the use of insulin shock treatment be made available for all schizophrenic patients until some more effective therapy is demonstrated.

That a statistically significant difference in length of stay in the hospital was found between the insulin-treated patients and patients not so treated is incontrovertible. However, from the data included in this report, the proposition that the insulin itself is the significant therapeutic factor would seem to be warranted only as a working hypothesis, rather than as a demonstrated fact. The main criteria used for evaluating effectiveness of treatment are length of hospitalization and level and stability of adjustment after discharge. While length of hospitalization is a focus of practical interest to state finance and the taxpayer, and while a legitimate reduction in the period of hospitalization is an economic desideratum in itself, it is not a definitive criterion for evaluating the precision of the insulin technic in effecting basic qualitative changes in the personality organization of schizophrenic patients and in the underlying patterns of emotional reaction from which the psychotic symptoms are derived. In actual practice, state hospitalization is resorted to for the schizophrenic patient when the family or the community can no longer tolerate his disturbed behavior and is terminated when the behavior has again come within the limits of tolerability. While an attempt is made in this study to evaluate qualitative differences in the effective level of posthospital adjustment, and differences favoring the insulin-treated group are found, they are small. For instance, in terms of gainful employment, a difference of only 10 per cent is noted between the insulin-treated patients and the patients not so treated. Actually, too, only 14 per cent more insulin-treated patients than non-insulin-treated patients were at home at the time this study was concluded, although 21 per cent more had been discharged. The figures for readmission are also of interest, 42 per cent of the insulin-treated patients having one or more readmissions to the hospital as compared with 31 per cent of the non-insulin-treated patients.

What the data in this study demonstrate is a positive relation between insulin shock treatment and a shortened stay in the hospital. In terms of hospital economy, it would be of interest to know what percentage of the total expenditure for the care of schizophrenic patients is represented by the saving of $80,274.60, given in this report only as an absolute figure. With the goal of increased economy in mind, some questions with regard to the control group not answered by the data in this report come to mind. For instance, how frequently was the possibility for discharge for patients in this group reviewed? May not days of hospitalization beyond the patients' actual needs have accumulated out of administrative cautiousness? That is, was each discharge in the control group actually made at the earliest possible date? It would also be of interest to have comparisons of the insulin group with a control group who received a comparable investment of trained psychotherapeutic attention.

The reviewer commends the method of approach employed in this study, particularly the inclusion of a control group. This in itself raises the study to a scientific level well above many statistical evaluations of insulin shock treatment. In the main this report is both thoughtful and thought-provoking and represents a valuable contribution to the literature of insulin shock therapy.

Pain. Research Publications, Association for Research in Nervous and Mental Disease. Vol. xxiii. Price, $7.50. Pp. 468, with 116 illustrations. Baltimore: Williams & Wilkins Company, 1943.

John Hilton, from his vast clinical experience, wrote about pain in 1876, and nearly seventy years later Sir Thomas Lewis from his vast clinical experience, wrote about pain. There is probably as much new information about pain in the volume under discussion which has accumulated in the year since the publication of Lewis' book as there was in all the years preceding.

Pain is a subjective phenomenon, and consequently does not lend itself well to animal experimentation. Hence, in the great majority of the papers collected in this volume man has been the subject of the experiments. One must pay tribute to the "pains-taking" attitude of both experimenters and subjects, since many of the experiments were obviously disagreeable and could have been carried out only for the purposes of extending the boundaries of knowledge.

New methods are ingeniously applied by means of which a sharp end point is attained, useful for the quantitative study of thresholds of pain. The differentiation

between the "bright" pain, carried by the large, rapidly conducting A fibers, and the "dull" pain, carried by the C fibers, is stated in fuller detail, and with precision, on the basis of superbly controlled experiments. The threshold of pain and the severity of the reaction to pain are differentiated, the former being relatively constant while the latter is much more variable. Sensations as they relate to pain, such as cold, heat, itching and pressure, are brought into the picture. Few of the authors would admit that the last word has been said. But methods have been devised to bring further information on pain to the man who deals in pain, the physician.

The second part of the volume takes up the locale, rather than the qualitative aspects, of pain. Here the discussion is more uneven, owing partly to the nature of the organ studied and partly to the preoccupations of the authors. Headache is particularly well covered, the contribution of the extracranial structures being adequately presented for the first time. The applied physiology that has blossomed as the result of the neurosurgical procedures is a welcome addition to knowledge of the mechanisms and pathways of pain.

In contrast to some of the other recent volumes of this series from the Association for Research in Nervous and Mental Disease, this volume is eminently readable and understandable.

Patients Have Families. By Henry B. Richardson. Price, $3. Pp. xx plus 408. New York: The Commonwealth Fund, 1945.

This book is the report of the director of an important investigation recently carried on by a group of health agencies in New York city. In it the relation of the patient to his family and his family background is surveyed from several angles. It has long been recognized that methods of obtaining information on this subject and its subsequent utilization are totally inadequate in the present practice of medicine. As the author, Dr. Henry B. Richardson, points out, only the old-fashioned general practitioner was in a position to evaluate the true nature of the patient's symptoms in relation to his family and background. Only the psychiatrist is at present equipped to analyze the material and to put it to therapeutic use.

The investigation of the family background of a number of patients seen in the wards and clinic of a city hospital was made with the cooperation of physicians, psychologists, social workers and public health nurses. Many organizations took part in the project, which was carried out over a number of years. For the most part the results are reported in the book through case or family histories. In parts of the book the "family as the unit of illness" and the "family as the unit of treatment" are considered. There is then a discussion of the present and of the future, in which there may be better utilization of the family unit in hospital and medical practice through cooperation of the various medical specialty units. In the case histories one finds concrete examples of the failure of medical practice of today because of inadequate utilization of background material related to the patient.

The author is to be complimented both on the detailed demonstration of the nature of the defects and on the suggestions for future improvement. Not only are practical details elaborated, but there is a scholarly discussion of earlier psychologic and sociologic material related to the subject in which he describes the homeostasis of the family group. The bibliography is excellent and draws from a wide field.

Neurology of the Eye, Ear, Nose and Throat. By E. A. Spiegel and I. Sommer. Price, $7.50. Pp. xi plus 667, with 117 illustrations. New York: Grune & Stratton, Inc., 1944.

This book may best be termed an uneven production. Spiegel and Sommer have attempted to do in one volume what Wilbrand and Saenger carried out in six volumes for the eye, and Alexander and Marburg in four volumes for the ear. Even the bibliography is overweighted, with over 1,700 references—far too many for a work of this size. Spiegel's wide acquaintance with the physiology of the nervous system appears on nearly every page, but his meticulousness gets him in trouble with the reader because of the frequent balancing of negative and positive results in complex experiments. Furthermore, the authors cannot seem to keep physiology in the background when they come to discuss clinical applications. It is as though they thought that even if the clinical results are not definite they should be because experimental work gives clearcut results. Aside from Spiegel's own original contributions to the neurology of the eye and ear, this must be considered as a scholastic rather than a scholarly work. There is a vast amount of information contained in the book, together with suitable illustrations, but the information is imperfectly digested. Possibly the book represents an attempt to get away from the oversimplification of neurology. If so, it has succeeded admirably.

News and Comment

APPOINTMENT OF DR. LEO M. DAVIDOFF

Dr. Leo M. Davidoff has been appointed attending neurologic surgeon at Montefiore Hospital for Chronic Diseases, New York, and will commence his duties on a full time basis on or about September 1. He has also been appointed to the rank of professor of clinical neurologic surgery at Columbia University College of Physicians and Surgeons.

Dr. Davidoff will continue with his consulting practice in neurosurgical problems at his office, which will be located in Montefiore Hospital.

Dr. Davidoff served as resident in neurologic surgery under Dr. Harvey Cushing in Boston and was later affiliated with the Neurological Institute of New York. Before coming to Montefiore Hospital, he was chief of surgery and attending neurologic surgeon at the Jewish Hospital of Brooklyn.